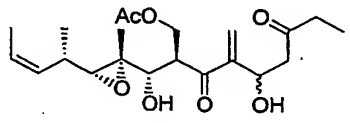
TOTAL SYNTHESIS OF MYRIAPORONES

The present invention relates to new myriaporones analogues and their use for the treatment of cancer. The present invention also relates to a total synthesis of myriaporones and derivatives.

BACKGROUND OF THE INVENTION

Myriaporones are a new class of marine polyketide-derived isolated from the bryozoan *Myriapora truncata*.



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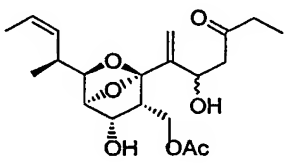

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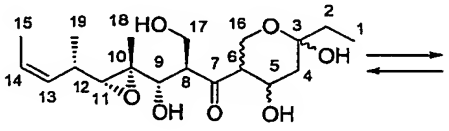

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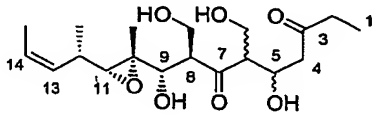

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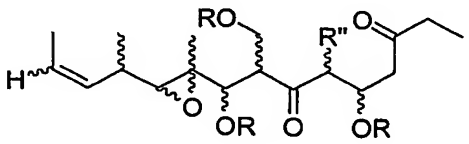
Myriaporones are disclosed to have antitumor activity. The complete structure for these related compounds was given by K. L. Rinehart *et al.*, *J. Nat. Prod.* **1995**, *58*, 344 and U.S. Patent No. 5,514,708. Myriaporones **3** and **4** described there are in an equilibrium mixture between the free hydroxy ketone and the hemiketal as indicated in the figure above.

There have been several unsuccessful attempts at the synthesis of myriaporones, see for example Taylor, R. E.; Ciavarri, J. C.; Hearn, B. R. "A Divergent Approach the Myriaporones and Tedanolide: Enantioselective Preparation of the Common Intermediate" *Tetrahedron Lett.* **1998**, *39*, 9361; Taylor *et al.*, *Org. Lett.* **2002**, *4*, 2853, available on the Web 02 August 2002.

In view of their interesting biological properties there is a need to provide an efficient, stereocontrolled total synthesis of myriaporones and related compounds.

SUMMARY OF THE INVENTION

In a first aspect, the present invention is directed to compounds of general formula I or a pharmaceutically acceptable salt, derivative, prodrug or stereoisomer thereof



(I)

wherein the substituent groups defined by R are each independently selected from the group consisting of H, SiR'_3, SOR′, SO_2R', C(=O)R′, C(=O)OR′, C(=O)NR′, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aryl, heteroaryl or aralkyl;

the group R' is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aminoalkyl, aryl, aralkyl and heterocyclic groups; and

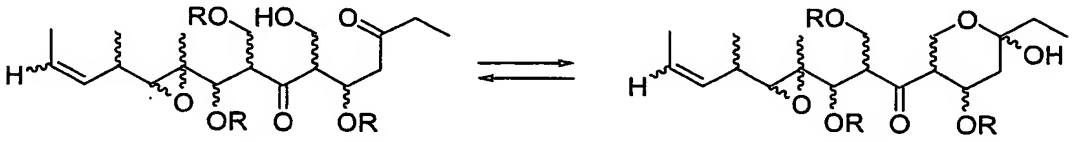
the group R'' is selected from the group consisting of H, OH, OR′, OCOR', SH, SR′, SOR′, SO_2R', NO_2, NH_2, NHR′, $N(R')_2$, NHCOR′, $N(COR')_2$, $NHSO_2R'$, CN, halogen, C(=O)H, C(=O)R′, CO_2H, CO_2R', CH_2OR, substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkylidene, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl and substituted or unsubstituted heteroaromatic;

with the proviso that the compound is not compound 1, 3 or 4 of US 5,514,708.

Compound 1 of US 5,514,708 corresponds to formula 1 shown above in the description of the prior art.

According to our findings, the natural compounds 3 and 4 of US 5,514,708 correspond to compounds 4a and 3a as described in the examples below.

When R'' is CH_2OH compounds of formula I may exist as a mixture of the ketone isomer and the hemiketal isomer (**5**),



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wherein the substituent groups defined by R are as defined above.

In particular, we prefer that at least one of the R substituents is not hydrogen. We have found that these compounds show improved cytotoxicity.

Myriaporones are obtained from natural sources. Another objective of the present invention is to provide a synthetic route to produce myriaporones and derivatives. Therefore, the present invention is directed to the synthesis of the compounds of formula I as defined above, including those where all R groups are H, and to intermediates used in the synthetic process.

According to the present invention, a process of this invention involves removing a protecting group from a compound of formula **5a** wherein at least one group R is a protecting group to give the corresponding compound of formula **5b** where the said at least one group R is hydrogen. This synthetic route can be applied to new and known myriaporones.

Another embodiment of the present invention is a pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt, derivative, prodrug or stereoisomer thereof or an intermediate of their synthesis and a pharmaceutically acceptable carrier.

Another embodiment of the present invention is the use of compounds of formula I or pharmaceutically acceptable salts, derivatives, prodrugs or stereoisomers thereof as antitumor agents.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to compounds of formula I as defined above.

In these compounds the substituents can be selected in accordance with the following guidance:

Alkyl groups preferably have from 1 to 12 carbon atoms. One more preferred class of alkyl groups has 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbon atoms, and most preferably 1, 2, 3 or 4 carbon atoms. Methyl, ethyl and propyl including isopropyl are particularly preferred alkyl groups in the compounds of the present invention. As used herein, the term alkyl, unless otherwise modified, refers to both cyclic and noncyclic groups, although cyclic groups will comprise at least three carbon ring members.

Preferred alkenyl and alkynyl groups in the compounds of the present invention have one or more unsaturated linkages and from 2 to about 12 carbon atoms, more preferably 2 to about 8 carbon atoms, still more preferably 2 to about 6 carbon atoms, even more preferably 2, 3 or 4 carbon atoms. The terms alkenyl and alkynyl as used herein refer to both cyclic and noncyclic groups, although straight or branched noncyclic groups are generally more preferred.

Alkylidene groups may be branched or unbranched and preferably have from 1 to 12 cabon atoms. One more preferred class of alkylidene groups has from 1 to about 8 carbon atoms, yet more preferably from 1 to about 6 carbon atoms, and most preferably 1, 2, 3 or 4 carbon atoms. Methylidene, ethylidene and propylidene including isopropylidene are particularly preferred alkylidene groups in the compounds of the present invention

Preferred alkylsulfinyl groups in the compounds of the present invention include those groups having one or more sulfoxide (SO) groups and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferably 1 to about 6 carbon atoms. Alkylsulfinyl groups having 1, 2, 3 or 4 carbon atoms are particularly preferred.

Preferred alkylsulfonyl groups in the compounds of the present invention include those groups having one or more sulfonyl (SO_2) groups and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferably 1 to about 6 carbon atoms. Alkylsulfonyl groups having 1, 2, 3 or 4 carbon atoms are particularly preferred.

Preferred aminoalkyl groups include those groups having one or more primary, secondary and/or tertiary amine groups, and from 1 to about 12 carbon atoms, more preferably 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbon atoms, even more preferably 1, 2, 3 or 4 carbon atoms. Secondary and tertiary amine groups are generally more preferred than primary amine moieties.

Suitable heterocyclic groups include heteroaromatic and heteroalicyclic groups. Suitable heteroaromatic groups in the compounds of the present invention contain one, two or three heteroatoms selected from N, O or S atoms and include, e.g., coumarinyl including 8-coumarinyl, quinolinyl including 8-quinolinyl, pyridyl, pyrazinyl, pyrimidyl, furyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, indolyl, benzofuranyl and benzothiazol. Suitable heteroalicyclic groups in the compounds of the present invention contain one, two or three heteroatoms selected from N, O or S atoms and include, e.g., tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, morpholino and pyrrolindinyl groups.

Suitable aryl groups in the compounds of the present invention include single and multiple ring compounds, including multiple ring compounds that contain separate and/or fused aryl groups. Typical aryl groups contain from 1 to 3 separated or fused rings and from 6 to about 18 carbon ring atoms. Specifically preferred aryl groups

include substituted or unsubstituted phenyl, naphthyl, biphenyl, phenanthryl, and anthracyl.

References herein to substituted groups in the compounds of the present invention refer to the specified moiety, typically alkyl or alkenyl, that may be substituted at one or more available positions by one or more suitable groups, e.g., halogen such as fluoro, chloro, bromo and iodo; cyano; hydroxyl; nitro; azido; carboxamido; alkyl groups including those groups having 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms and more preferably 1-3 carbon atoms; alkenyl and alkynyl groups including groups having one or more unsaturated linkages and from 2 to about 12 carbon or from 2 to about 6 carbon atoms; alkoxy groups having those having one or more oxygen linkages and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; aryloxy such as phenoxy; alkylthio groups including those moieties having one or more thioether linkages and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; alkylsulfinyl groups including those moieties having one or more sulfinyl linkages and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; alkylsulfonyl groups including those moieties having one or more sulfonyl linkages and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; aryl having 6 or more carbons, particularly phenyl; aralkyl such as benzyl; heterocyclic groups including heteroalicyclic and heteroaromatic groups, especially with 5 to 10 ring atoms of which 1 to 4 are heteroatoms, more preferably heterocyclic groups with 5 or 6 ring atoms and 1 or 2 heteratoms or with 10 ring atoms and 1 to 3 heteroatoms.

Preferred R groups include alkyl, alkenyl and alkynyl that may be substituted at one or more available positions by one or more suitable groups, e.g., halogen such as fluoro, chloro, bromo and iodo, especially ω-chloro or perfluoro; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 carbon atoms, preferably from 1 to about 6 carbon atoms; aryl having 6 or more carbons, particularly phenyl; aralkyl such as benzyl; heterocyclic groups including heteroalicyclic and heteroaromatic groups, especially with 5 to 10 ring atoms of which 1 to 4 are heteroatoms, more preferably heterocyclic groups with 5 or 6 ring atoms and 1 or 2 heteratoms or with 10

ring atoms and 1 to 3 heteroatoms, the heterocyclic groups optionally being substituted with one or more of the substituents, especially amino such as dimethylamino or with keto.

The term "pharmaceutically acceptable salts, derivatives, prodrugs" refers to any pharmaceutically acceptable salt, ester, solvate, hydrate or any other compound which, upon administration to the recipient is capable of providing (directly or indirectly) a compound as described herein. However, it will be appreciated that non-pharmaceutically acceptable salts also fall within the scope of the invention since those may be useful in the preparation of pharmaceutically acceptable salts. The preparation of salts, prodrugs and derivatives can be carried out by methods known in the art.

For instance, pharmaceutically acceptable salts of compounds provided herein are synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts are, for example, prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent or in a mixture of the two. Generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol or acetonitrile are preferred. Examples of the acid addition salts include mineral acid addition salts such as, for example, hydrochloride, hydrobromide, hydroiodide, sulphate, nitrate, phosphate, and organic acid addition salts such as, for example, acetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, methanesulphonate and p-toluenesulphonate. Examples of the alkali addition salts include inorganic salts such as, for example, sodium, potassium, calcium and ammonium salts, and organic alkali salts such as, for example, ethylenediamine, ethanolamine, N,N-dialkylenethanolamine, triethanolamine and basic aminoacids salts.

The compounds of the invention may be in crystalline form either as free compounds or as solvates (e.g. hydrates) and it is intended that both forms are within the scope of the present invention. Methods of solvation are generally known within the art.

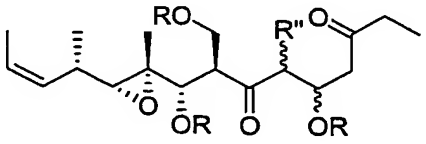
Any compound that is a prodrug of a compound of formula I is within the scope and spirit of the invention. The term "prodrug" is used in its broadest sense and encompasses those derivatives that are converted in vivo to the compounds of the

invention. Such derivatives would readily occur to those skilled in the art, and include, for example, compounds where a free hydroxy group is converted into an ester derivative.

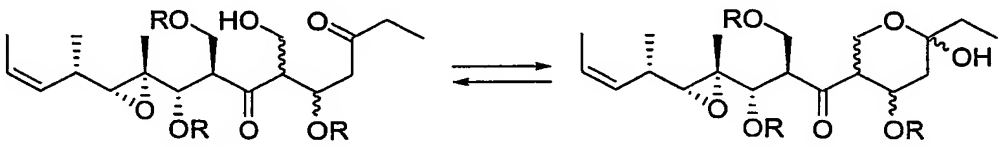
The compounds of the present invention represented by the above described formula **I** may include enantiomers depending on their asymmetry or diastereoisomers. The single isomers and mixtures of the isomers fall within the scope of the present invention.

In one aspect, the present invention extends to compounds of formula **I** which differ from the known myriaporones in respect of one or more positions of stereochemistry. Thus, in this aspect, the compounds are isomers and isomeric derivatives.

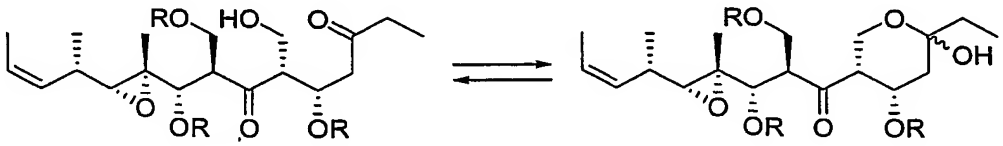
The preferred stereochemistry of compounds of formula **I** is the following:



When R'' is CH_2OH the preferred stereochemistry of compounds of formula **5** is:



Particularly preferred are compounds having the following stereochemistry:

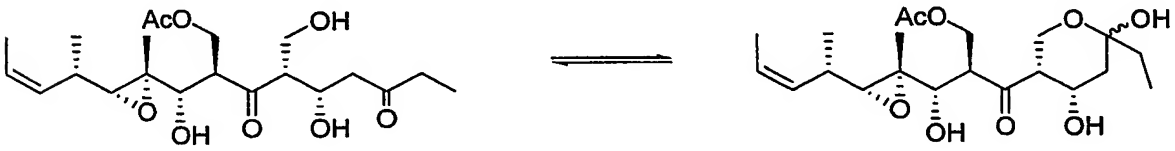


and

We have found that these particular groups of compounds show improved biological properties.

In another preferred embodiment of the present invention, R" is a substituted or unsubstituted alkylidene.

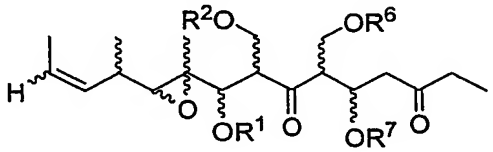
In one preferred embodiment of the compounds of formula 5, at least one of the R substituents is C(=O)R'. Particularly preferred is the compound of formula **47**:



47

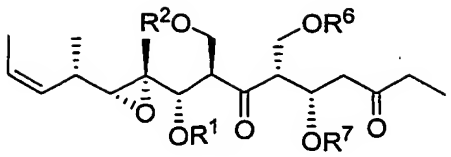
In another embodiment of the compounds of formula **I** or of formula **5**, at least one of the R substituents is not hydrogen. Suitably, each group that is not hydrogen is a protecting group, which may be the same or different.

Compounds of the following formula are preferred:



where R^1, R^2, R^6 and R^7 are hydroxy protecting groups.

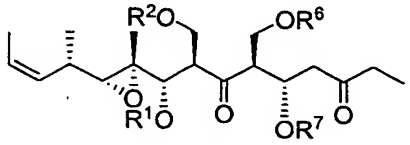
Particularly preferred are compounds of formula **19**:



19

where R^1, R^2, R^6 and R^7 are hydroxy protecting groups;

and of formula **30**:



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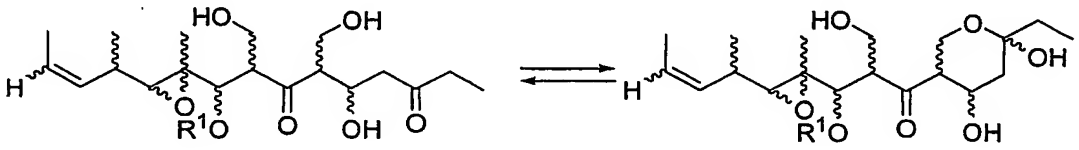
where R^1, R^2, R^6 and R^7 are hydroxy protecting groups.

Suitably, R^1, R^2, R^6 and R^7 are the same protecting group. They can be chosen from TBS ($tBuMe_2Si$-), TBDPS ($tBuPh_2Si$-), TES (Et_3Si-), MOM (CH_3OCH_2-), MEM ($CH_3OCH_2CH_2OCH_2$-), SEM ($(CH_3)_3SiCH_2CH_2OCH_2$-) and Ac- (CH_3CO-). Especially preferred is TBS ($tBuMe_2Si$-) or TBDPS ($tBuPh_2Si$-).

Also preferred are compounds of the following formula:



where R^1 is a hydroxy protecting group.

Particularly preferred are compounds of formula **20** and **31**:

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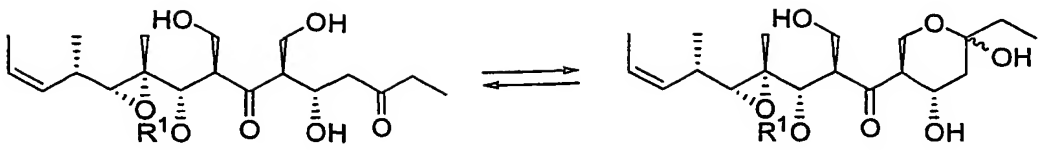
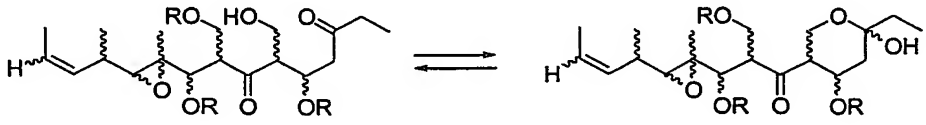


31

In the above compounds, R^1 is suitably TBS ($tBuMe_2Si$-).

The present invention also provides a process for synthesis of a myriaporone compound of formula **5**:



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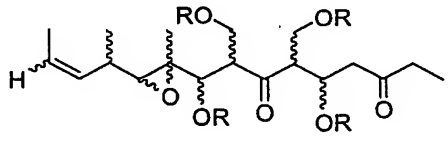
which may exist as a mixture of the ketone isomer and the hemiketal isomer, or as one of the two isomeric forms;

wherein the substituent groups defined by R are each independently selected from the group consisting of H, SiR'_3, SOR', SO_2R', $C(=O)R'$, $C(=O)OR'$, $C(=O)NR'$, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aryl, heteroaryl or aralkyl, and wherein at least one group R is hydrogen;

and wherein the group R' is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aminoalkyl, aryl, aralkyl and heterocyclic groups;

which comprises removing a protecting group from an intermediate compound of formula:

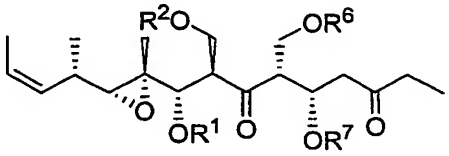


wherein the substituent groups defined by R are each independently selected from the group consisting of H, SiR'_3, SOR', SO_2R', $C(=O)R'$, $C(=O)OR'$, $C(=O)NR'$, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aryl, heteroaryl or aralkyl, and wherein the or each group R to become hydrogen in the compound **5** is in the intermediate compound protecting group;

and wherein the group R' is as defined.

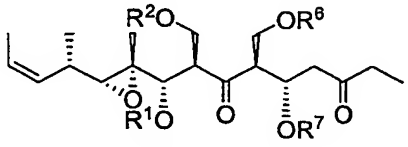
Suitably, more than one group R in the intermediate compound is a protecting group.

A process of this invention can comprise removing at least one protecting group from a compound of formula **19**:



where R^1, R^2, R^6 and R^7 are hydroxy protecting groups.

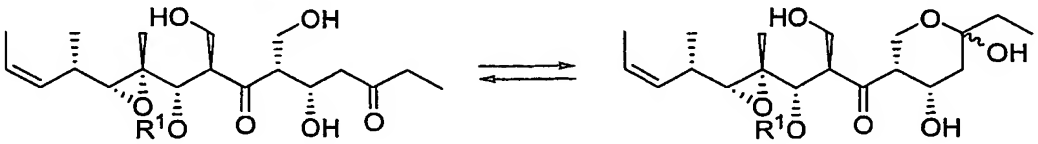
A related process of this invention can comprise removing at least one protecting group from a compound of formula **30**:



where R^1, R^2, R^6 and R^7 are hydroxy protecting groups.

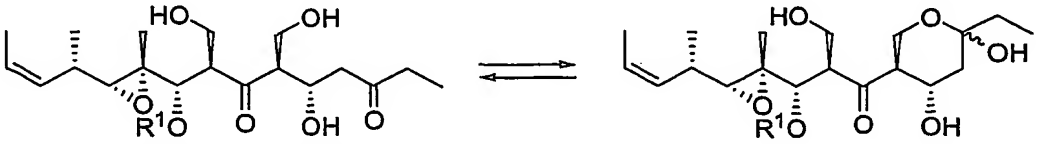
Suitably R^1, R^2, R^6 and R^7 are the same protecting group and are removed.

Another process of this invention comprises removing a protecting group from a compound of formula **20**:



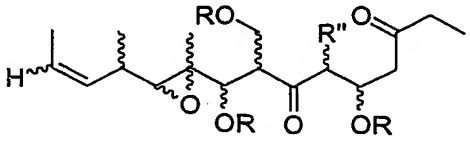
where R^1 is a hydroxy protecting group.

A related process comprises removing a protecting group from a compound of formula **31**:



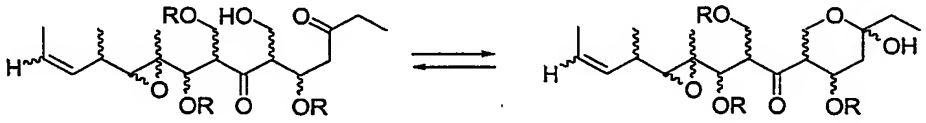
where R^1 is a hydroxy protecting group.

The invention further provides a process for synthesis of a myriaporone compound of formula **I**:



(I)

wherein the substituent groups R and R" are as defined above for the formula **I**;
which comprises derivatisation of a compound of formula **5**:



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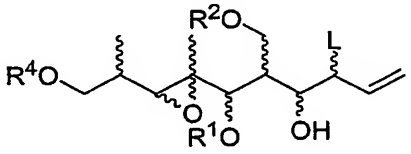
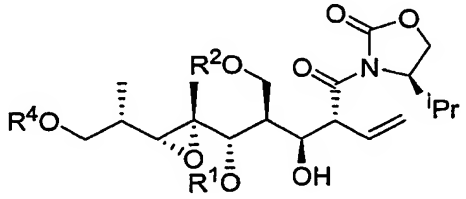
which may exist as a mixture of the ketone isomer and the hemiketal isomer, or as one of the two isomeric forms;
and wherein the substituent groups are as defined in claim 25.

The invention further provides compounds of the following formula



where R^1, R^2 and R^4 are hydroxy protecting groups, and L is a stereospecific leaving group which induces chirality.

Preferred are compounds of formula **10** and **22**:



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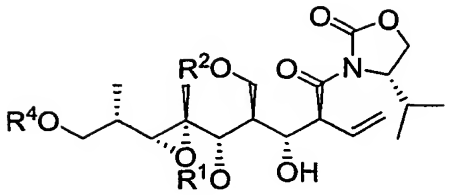
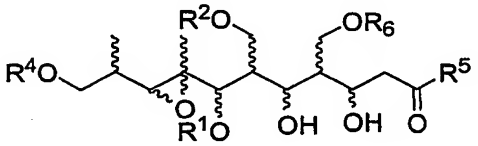


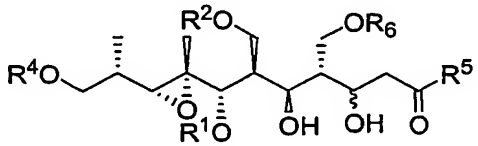
22

The invention also provides compounds of the following formula:

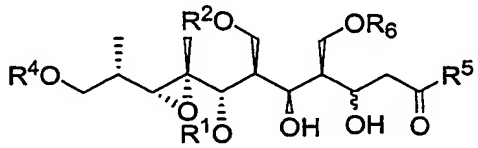


wherein R^1, R^2, $R^4$and R^6 are hydroxy protecting groups;
R^5 is selected from the group consisting of H, SOR′, SO_2R', C(=O)R′, C(=O)OR′, C(=O)NR′, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aryl, heteroaryl or aralkyl;
and R' has the same meaning as defined in claim 1.

Preferred are compounds of formula **14** and **26**:



14

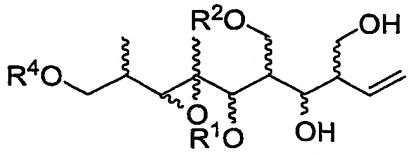


26

The invention also provides a process for preparation of a compound of formula **14** which comprises chain extension of a compound of formula **13**; a process for preparation of a compound of formula **26** which comprises chain extension of a compound of formula **25**; a process for preparation of a compound of formula **19** which

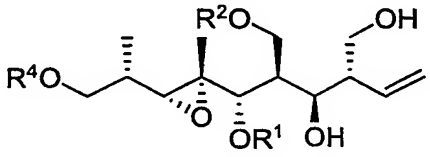
comprises chain extension of a compound of formula **18**; and a process for preparation of a compound of formula **30** which comprises chain extension of a compound of formula **29**.

The invention also provides compounds of the following formula:

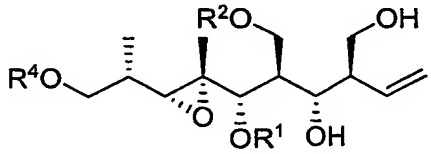


wherein R^1, R^2 and R^4 are hydroxy protecting groups.

Preferred are compounds of formula **11** and **23**:

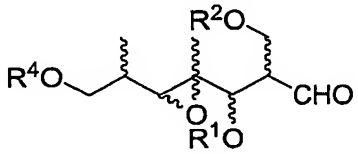


11



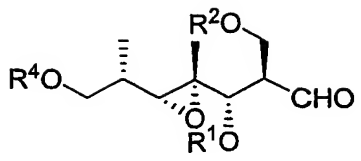
23

The invention also provides compounds of the following formula:



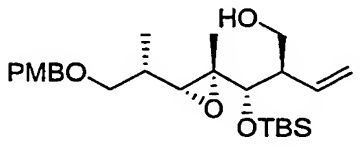
wherein R^1, R^2 and R^4 are hydroxy protecting groups.

Compounds of formula **8** are preferred:



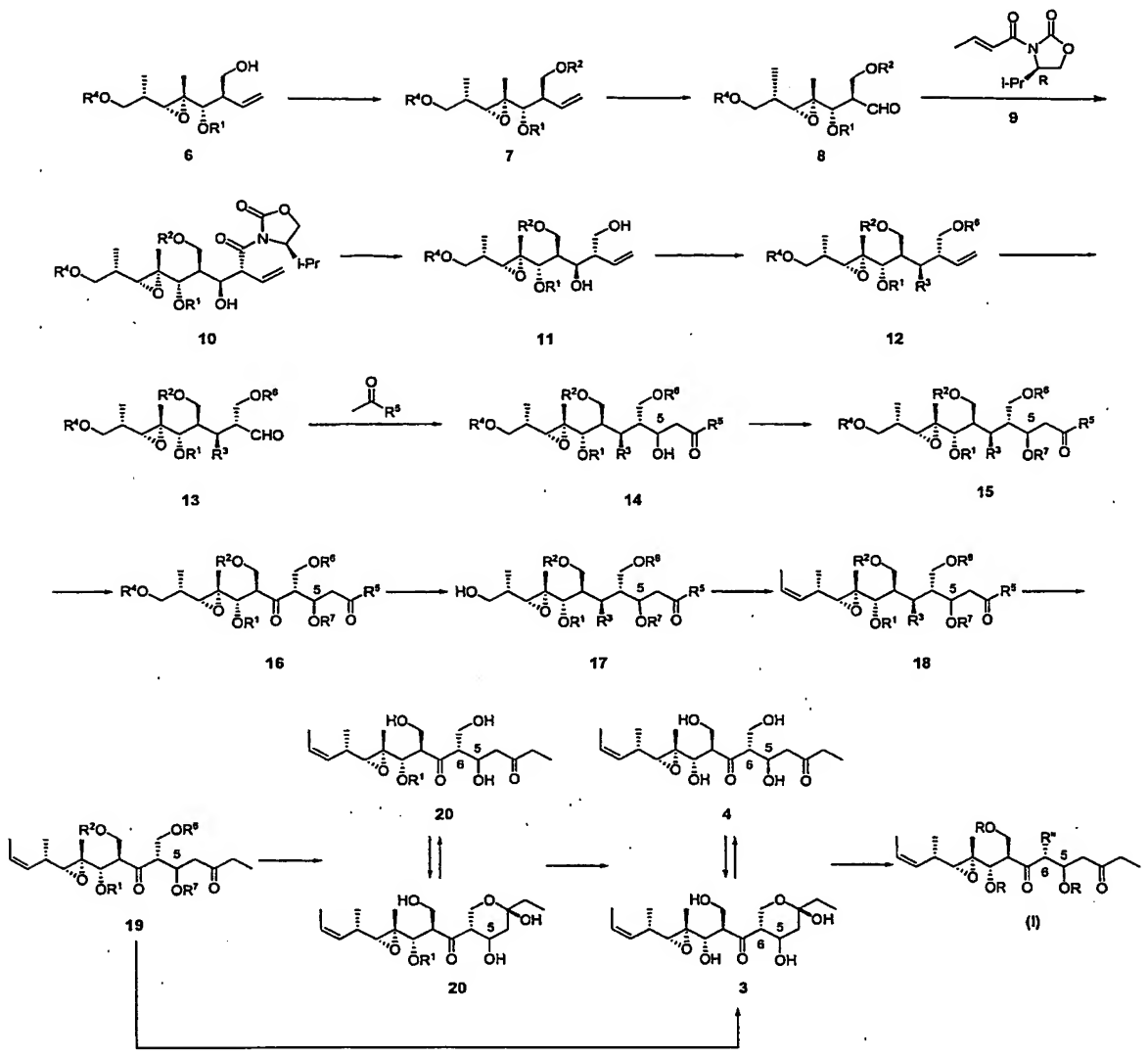
8

The compounds of the present invention can be synthetically prepared from the intermediate compound **6** described by W. R. Roush *et al.*, *Org. Lett.* **1999**, *1*, 95 or its stereoisomers.



6

A method of producing compounds of formula **I** is shown in the **Scheme 1**.



Scheme 1

For the purpose of discussing this scheme, the carbons in each respective molecule are assigned with the appropriate number to their final position at the end product of formula **I**, using the numbering system given previously for the known compound **3/4**. The scheme 1 involves:

- protecting the compound **6** to give protected compound **7**. This protection is carried out with the related reagent of the selected protecting group (such as TBSCl, TESOTf, MOMBr or $tBu_2Si(OTf)_2$) in the conditions according to known procedures in organic synthesis (for example: Imidazole, DIPEA or 2,6-lutidine in DMF or CH_2Cl_2), alternative protecting groups are also contemplated,

- converting the terminal vinyl group at carbons 6 and 7 to an aldehyde in compound **8**. This conversion is carried out by ozonolysis of the vinyl group (for example with O_3, in CH_2Cl_2 at –78 °C) or by formation of the corresponding dihydroxy derivative (for example with NMO, OsO_4 in THF:H_2O) and the diol is cleavaged (for example with $NaIO_4$ in THF:H_2O) to the corresponding aldehyde,

- reaction with an oxazolidinone **9** to give compound **10**. The oxazolidinone **9** is converted into the corresponding enolate (for example with Bu_2BOTf and Et_3N in CH_2Cl_2 at –78 °C) and added to **8** at low temperature (-30 °C) to give **10**. Other stereospecific leaving groups which induce the desired chirality are also contemplated within the scope of protection of the invention.

- reduction of compound **10** to obtain a 17-hydroxymethyl sidechain in the compound **11**. This reduction is carried out with the corresponding reagent (such as $LiBH_4$) in the conditions (for example in THF:H_2O or CH_2Cl_2) according to known procedures in organic synthesis, although other reducing agents are also contemplated within the scope of protection of the invention.

- further protection at the 17-hydroxy group to give compound **12**. This protection is carried out with the related reagent of the selected protecting group (such as TBSCl, TESCl, MEMCl or SMCl) in the conditions according with known procedures in organic synthesis (for example: Imidazole, DIPEA, DMAP or Et_3N in DMF or CH_2Cl_2), other protecting groups are also contemplated in the invention,

- converting the terminal vinyl group at carbons 4 and 5 to an aldehyde in compound **13**. This conversion is carried out by ozonolysis of the vinyl group (for example O_3, in CH_2Cl_2 at –78 °C) or by formation of the corresponding dihydroxy derivative (for example NMO, OsO_4 in THF:H_2O) and the diol was cleavaged (for example $NaIO_4$ in THF:H_2O or $Pb(OAc)_4$ in toluene) to the corresponding aldehyde,

- chain extension at carbon 5 to give compound **14**. In the illustrated example, the selected reagent ($CH_3C(O)N(CH_3)OCH_3$) is converted into the corresponding enolate ($[(CH_3)_3Si]_2NLi$ in THF at –78 °C) and added to **13** at low temperature (-78 °C) to give

14, alternative procedures for chain extension known to the person skilled in the art can also be used to achieve the same purpose,

- further protection at the 5-hydroxy group to give compound **15**. This protection is carried out with the related reagent of the selected protecting group (such as TBSOTf) in the conditions (2,6-lutidine in CH_2Cl_2) according to known procedures. Alternative protecting groups can also be used,

- oxidation of the hydroxy group at carbon 7 to afford compound **16**. This oxidation is carried out with the corresponding reagent (such as Dess-Martin periodinane) in the conditions according with known procedures in organic synthesis (for example in CH_2Cl_2),

- deprotection at the 13-protected hydroxy group to give terminally deprotected compound **17**. This deprotection is carried out with the related reagent (for example DDQ) for the selected protecting group (for example PMB) in the conditions according with known procedures (for example in CH_2Cl_2:H_2O),

- formation of a terminal olefin group by extension with carbons 14 and 15 to give compound **18**. This transformation is performed in two steps: a) oxidation of the primary hydroxy group into the corresponding aldehyde with the selected reagent (for example Dess-Martin periodinane) and b) formation of the *cis* double bound through a Wittig or Horner-Wadsworth-Emmons reaction in the standard conditions, alternative procedures for chain extension known to the person skilled in the art can also be used to achieve the same purpose,

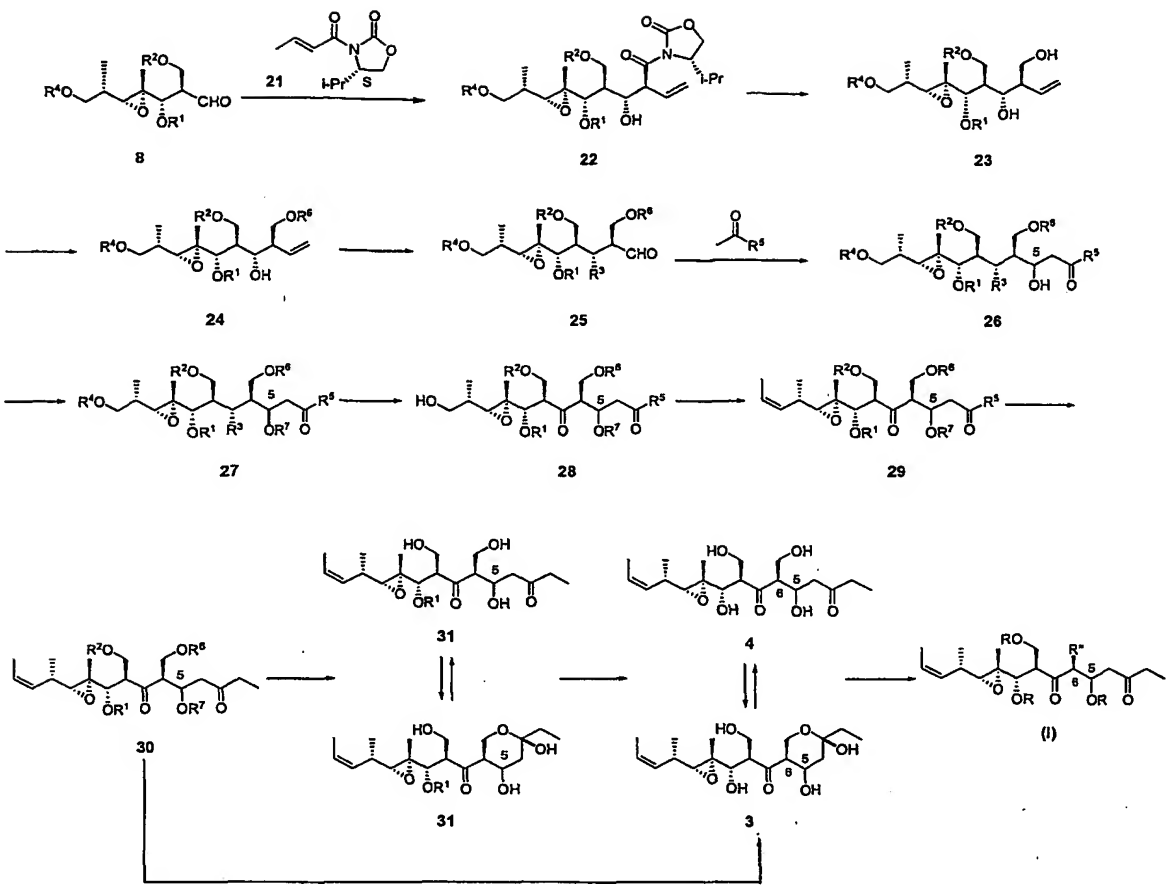
- formation, if not already present, of the 7-keto substituent of compound **19**. This oxidation is carried out with the corresponding reagent (such as Dess-Martin periodinane) in the conditions according with known procedures in organic synthesis (for example in CH_2Cl_2),

- chain extension with carbons 1 and 2 if not already present in compound **19**. This extension is carried out with the corresponding reagent (such as BrMgEt) in the conditions according with known procedures in organic synthesis (for example in THF),

- partial or complete deprotection to a compound **20** or **4/3**. This deprotection is carried out with the related reagent (such as TBAF and AcOH) for the selected protecting group (for example TBS) in the conditions according with known procedures (for example in CH_2Cl_2),

- and optional derivatisation to a derivative shown as compound **(I)**, where at least one R is not hydrogen, for example by reaction with Ac_2O, an alkylcarboxylate chloride or anhydride in the presence of the corresponding base (for example Et_3N) in any suitable solvent such as $CHCl_3$.

Additionally, different isomerically synthetic myriaporones are prepared from the intermediate compound **8** by using a different stereospecific leaving group, for example by using (S)-oxazolidinone instead of (R)-oxazolidinone. The route for producing these compounds is depicted in **Scheme 2**.



Scheme 2

The reaction scheme 2 involves the same reactions as those of scheme I, with a different stereochemistry in the oxazolidinone **9**.

A purpose of the invention is to provide a first total synthesis of myriaporones **3** and **4** and from these compounds or previous intermediates obtain other compounds of formula **I**. The synthesis should preferably make it possible to obtain the largest possible quantities of myriaporones **3** and **4** by simple ways and means. The synthesis should also allow the preparation of the largest possible number of specific derivatives of myriaporones **3** and **4**. In addition, the synthesis should preferably proceed stereoselectively, so that four diastereoisomers of myriaporones **3** and **4** can be obtained in pure form. A further purpose of the invention is to provide the kind of total synthesis intermediates that will make the synthesis as flexible as possible and thus enable the preparation of a large number of derivatives.

In the previous reaction schemes, the hydroxy protecting groups R^1, R^2, R^4, R^6, and R^7 may be any of the examples of hydroxy protecting groups reported in "Protective Groups in Organic Synthesis", T. W. Greene, P. G. Wuts, Ed. Wiley-Interscience, 3rd Edition. Examples of hydroxy protecting groups are given in the following list:

protection for -OH group	abbreviation
ethers	
methyl	
methoxymethyl	MOM
benzyloxymethyl	BOM
methoxyethoxymethyl	MEM
2-(trimethylsilyl)ethoxymethyl	SEM
methylthiomethyl	MTM
phenylthiomethyl	PTM
azidomethyl	
cyanomethyl	
2,2-dichloro-1,1-difluoroethyl	
2-chloroethyl	
2-bromoethyl	
tetrahydropyranyl	THP
1-ethoxyethyl	EE
phenacyl	
4-bromophenacyl	
cyclopropylmethyl	
allyl	
propargyl	
isopropyl	
cyclohexyl	
t-butyl	
benzyl	
2,6-dimethylbenzyl	
4-methoxybenzyl	MPM or PMB
o-nitrobenzyl	
2,6-dichlorobenzyl	
3,4-dichlorobenzyl	
4-(dimethylamino)carbonylbenzyl	
4-methylsuflinylbenzyl	Msib
9-anthrylmethyl	
4-picolyl	
heptafluoro-*p*-tolyl	
tetrafluoro-4-pyridyl	
trimethylsilyl	TMS
t-butyldimethylsilyl	TBDMS

t-butyldiphenylsilyl	TBDPS
triisopropylsilyl	TIPS

esters

aryl formate	
aryl acetate	
aryl levulinate	
aryl pivaloate	ArOPv
aryl benzoate	
aryl 9-fluorocarboxylate	

aryl methyl carbonate	
1-adamantyl carbonate	
t-butyl carbonate	BOC-OAr
4-methylsulfinylbenzyl carbonate	Msz-Oar
2,4-dimethylpent-3-yl carbonate	Doc-Oar
aryl 2,2,2-trichloroethyl carbonate	
aryl vinyl carbonate	
aryl benzyl carbonate	
aryl carbamate	

dimethylphosphinyl	Dmp-OAr
dimethylphosphinothioyl	Mpt-OAr
diphenylphosphinothioyl	Dpt-Oar

aryl methanesulfonate
aryl toluenesulfonate
aryl 2-formylbenzenesulfonate

Preferred R^2, R^4, R^6 and R^7 are TBS ($tBuMe_2Si$-), TBDPS ($tBuPh_2Si$-), TES (Et_3Si-), MOM (CH_3OCH_2-), MEM ($CH_3OCH_2CH_2OCH_2$-), SEM ($(CH_3)_3SiCH_2CH_2OCH_2$-) and Ac-, and more preferred are TBS and TBDPS. It is also preferred that R^2, R^4, R^6 and R^7 are the same protecting group. Preferred R^1 is PMB (p-MeO-Ph-CH_2-). The protecting and deprotecting reactions presented in previous reaction schemes are performed according to the state of the art.

The group R^3 shown in the schemes is selected from the group consisting of H, OH, =O, OR', OSiR', OSOR', OSO_2R', OCOR', OCOOR', CONR', NHR' and NR'R'. R' has the same meaning as defined in formula I. Preferred R^3 is a hydroxy or =O.

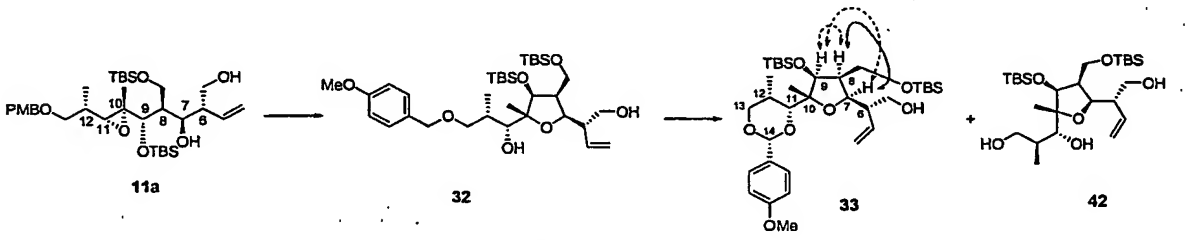
The group shown as R^5 in the schemes is selected from the group consisting of H, SOR', SO_2R', C(=O)R', C(=O)OR', C(=O)NR', substituted or unsubstituted alkyl,

substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, aryl, heteroaryl or aralkyl. And R' has the same meaning as defined in formula **I**. Preferred R^5 is C_1-C_6 and more preferred is ethyl.

The identity of compounds **9** and **21** can be changed obtaining for other ways compounds **11** and **23** from compound **8**, according to the state of the art.

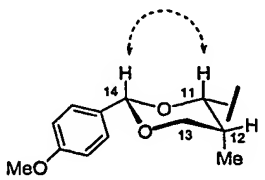
The relative stereochemistry at C-8-C-12 of compounds **3** and **4** was assumed as the same as described in Patent No. 5,514,708, **1996** on the basis of coupling constant comparisons cited there. Besides, the stereochemistry of the starting material **6** written above was already indicated by W. R. Roush *et al.*, *Org. Lett.* **1999**, 1, 95.

To support this information, the stereochemistry of these carbons was assigned on the basis of NOESY and COSY studies of the intramolecular epoxide opened product **33** which was prepared from **11a** in two steps (Scheme 3).



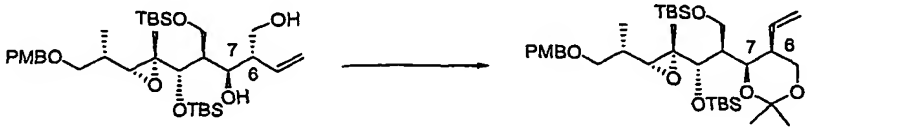
Scheme 3

The absolute configuration of C-8 to C-12 has been readily identified by NOE experiments. A syn relative stereochemistry at C-11-C-12 was deduced from the coupling constant (J= 1.5 Hz). A NOE signal between H-11 and H-14 indicates both must be in axial position.



33

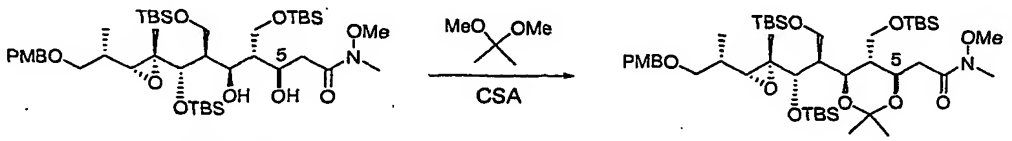
An anti relative stereochemistry at C-6-C-7 was deduced from the small value of the coupling constant of the acetonide **34** prepared from compound **11a** (Scheme 4).



11a **34** δ H-7 = 4.20 (dd, *J*= 4.2, 1.2 Hz, 1H)

Scheme 4

Finally, the stereochemistry of compounds **3a**, **3b**, **4a** and **4b** at C-5 was assigned by conversion of the 1,3 diol of **15a** and **15b** to the 1,3- syn and anti acetonides respectively (scheme 5).



15a = 5(S)
15b = 5(R)

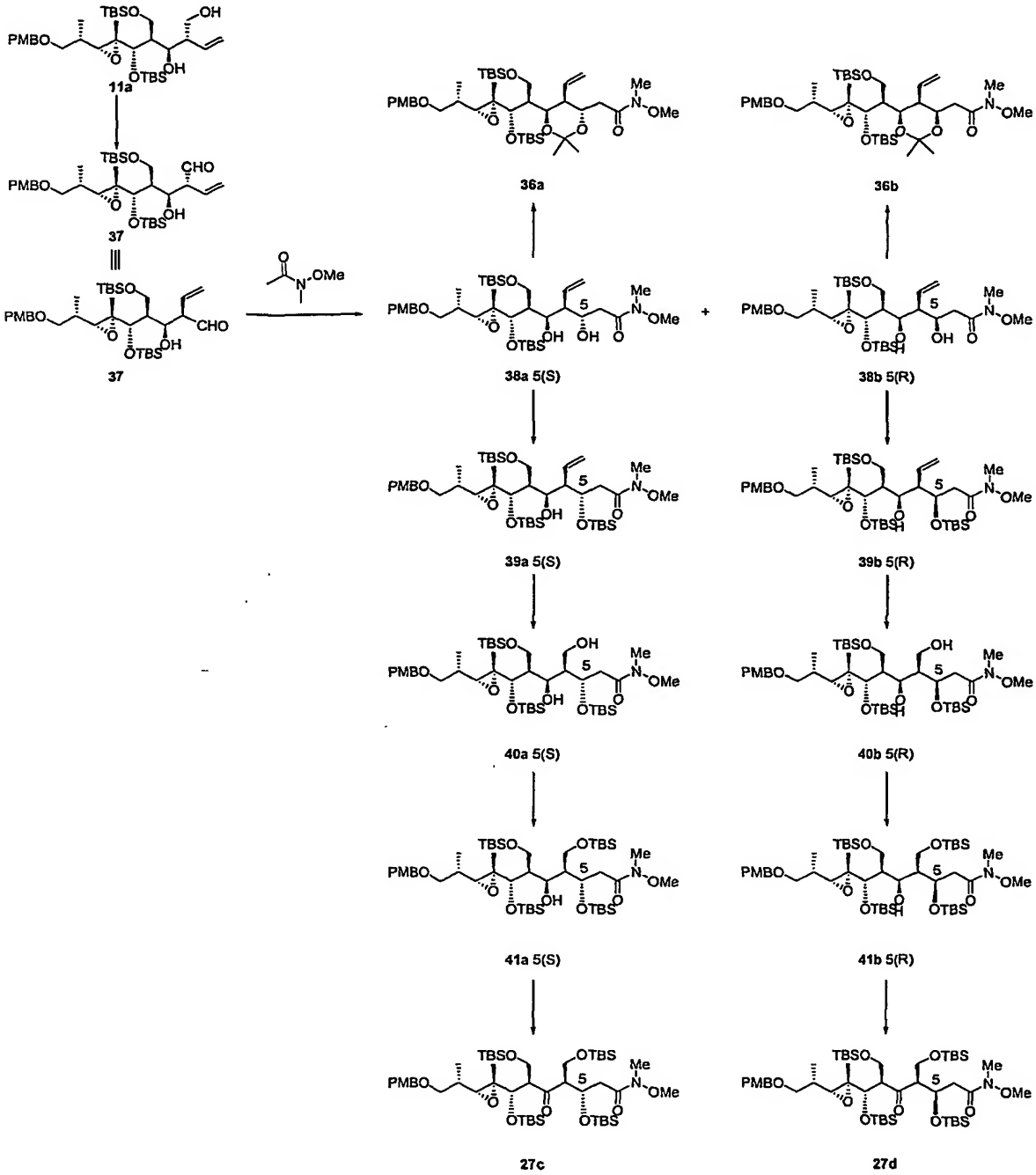
35a = 5(S)
35b = 5(R)

Scheme 5

The stereochemistry of syn- and anti- 1,3-diol acetonides was assigned according to S. D. Rychnovsky *et al.*, *J. Org. Chem.* **1993**, 58, 3511-3515, from the ^{13}C chemical shifts of the acetal methyl groups. In general, the syn-1,3-diol acetonides have acetal methyl shifts at 19 and 30 ppm respectively, while the anti-acetonides have both methyl shifts at about 25 ppm. Indeed, we have tested the reability of this method since the ^{13}C NMR spectrum of the syn-acetonide **35b** shows an axial methyl group at ca. 20.2 ppm and an equatorial methyl group at ca. 30.0 ppm, whereas the ^{13}C spectrum of the anti-acetonide **35a** shows both methyl groups at 24.4 and 25.2 ppm.

Unfortunately, it could not be possible to determine the stereochemistry of **3c**, **3d**, **4c** and **4d** by preparing the acetonides of **26a** and **26b** since these compounds could not be separate by conventional methods. In these cases, the configuration at C-5 position was stablished by conversion of **11a** into the 1,3-diols **38a** and **38b** which can be easily separated. After several reactions, these compounds are leaded to the known intermediates **27c** and **27d** respectively. The stereochemistry of these compounds was

determined from the ^{13}C chemical shifts of the corresponding acetonides **36a** (δ= 24.1, 25.0 ppm) and **36b** (δ= 19.7, 29.9 ppm) (scheme 6).



Scheme 6

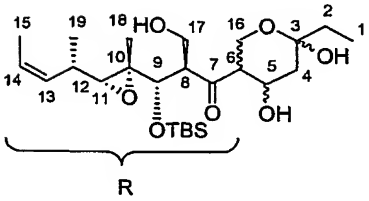
The relative stereochemistry for H-5 and H-6 at myriaporones 3 and 4 was concluded by studing the coupling constants between the protons on the six-membered rings hemiketal monoprotected myriaporones **20** and **31** (scheme 7).

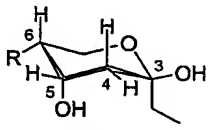
For **20a** and **31b**, H-4 at δ 1.73 and 1.58 ppm respectively, both with coupling constants of 14.5, 3.5 Hz was assigned to be axial. The others H-4 with upfield chemical shift at δ 2.02 and 2.03 ppm for each compound, have coupling constants of 14.0, 3.5 Hz and 14.5, 3.5 Hz, respectively. These value indicate the proton H-5 should be equatorial.

Similary, the coupling constants between H-5 and H-6 are, in both cases, around 2 Hz, indicating again that H-5 should be equatorial. Thus, the relative stereochemistry for H-5 and H-6 is concluded to be syn.

On the other hand, the ^{1}H NMR spectra of compounds **20b** and **31a** are different from compounds **20a** and **31b** in coupling constants and, primarily, in the chemical shift. For these compounds, the coupling constants between H-4 (ax) and H-5 are around 12, 13 Hz, indicating H-5 should be in axial.

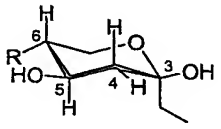
In addition, the coupling constants between H-5 and H-6 are in concordance with the fact that H-6 is placed in axial to minimize interaction and therefore, the relative stereochemistry for H-5 and H-6 is concluded to be anti.





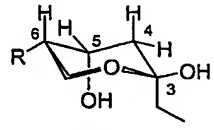
20a

H-4$_{ax}$ δ 1.73 (dd, J = 3, 14 Hz)
H-4$_{eq}$ δ 2.02 (dd, J = 3.5, 14 Hz)
H-5$_{eq}$ δ 4.79 (d, J = 2.5 Hz)
H-6$_{ax}$ δ 2.77 (ddd, J = 2.5, 5, 11.5 Hz)



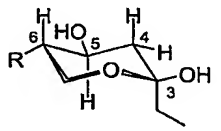
20b

H-4$_{ax}$ δ 1.46 (dd, J = 12, 13 Hz)
H-4$_{eq}$ δ 2.08 (dd, J = 5, 12.5 Hz)
H-5$_{ax}$ δ 4.38 (ddd, J = 5, 11.5, 15.5 Hz)
H-6$_{ax}$ δ 2.77 (ddd, J = 4.5, 11, 14.5 Hz)



31b

H-4$_{ax}$ δ 1.58 (dd, J = 3, 14 Hz)
H-4$_{eq}$ δ 2.03 (dd, J = 3.5, 14.5 Hz)
H-5$_{eq}$ δ 4.62 (bs)
H-6$_{ax}$ δ 2.94 (ddd, J = 2, 5, 11.5 Hz)



31a

H-4$_{ax}$ δ 1.46 (dd, J = 11.5, 13 Hz)
H-4$_{eq}$ δ 2.09 (dd, J = 4.5, 12.5 Hz)
H-5$_{ax}$ δ 4.79 (ddd, J = 4.5, 11, 12.6 Hz)
H-6$_{ax}$ δ 2.77 (ddd, J = 5.5, 11, 17.5 Hz)

Scheme 7

The stereochemistry at C-3 in the hemiketal compounds could not be assigned by NOE experiments. In the scheme 7, the hemiketal hidroxi group at C3 was arbitrarily placed equatorial.

Another especially preferred embodiment of the present invention is pharmaceutical compositions useful as antitumor agents which contain as active ingredient a compound or compounds of the invention, as well as the processes for their preparation.

An important feature of the above described compounds of formula I is their bioactivity and in particular their cytotoxic activity. With this invention we provide novel pharmaceutical compositions of compounds of general formula I that possess cytotoxic activity, and their use as antitumor agents. Thus the present invention further provides pharmaceutical compositions comprising a compound of this invention, a pharmaceutically acceptable salts, derivatives, prodrugs or stereoisomers thereof with a pharmaceutically acceptable carrier.

Examples of pharmaceutical compositions include any solid (tablets, pills, capsules, granules etc.) or liquid (solutions, suspensions or emulsions) with suitable composition for oral, topical or parenteral administration.

Administration of the compounds or compositions of the present invention may be any suitable method, such as intravenous infusion, oral preparation, intraperitoneal and intravenous preparation. We prefer that infusion times of up to 24 hours are used, more preferably 2-12 hours, with 2-6 hours most preferred. Short infusion times which allow treatment to be carried out without an overnight stay in hospital are especially desirable. However, infusion may be 12 to 24 hours or even longer if required. Infusion may be carried out at suitable intervals of say 1 to 4 weeks. Pharmaceutical compositions containing compounds of the invention may be delivered by liposome or nanosphere encapsulation, in sustained release formulations or by other standard delivery means.

The correct dosage of the compounds will vary according to the particular formulation, the mode of application, and the particular situs, host and tumour being treated. Other factors like age, body weight, sex, diet, time of administration, rate of excretion, condition of the host, drug combinations, reaction sensitivities and severity of the disease shall be taken into account. Administration can be carried out continuously or periodically within the maximum tolerated dose.

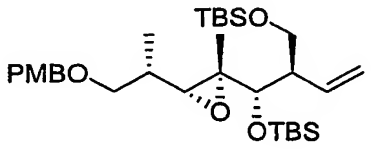
The compounds and compositions of this invention may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time or a different time.

Antitumoral activities of these compounds include among others leukaemias, lung cancer, colon cancer, kidney cancer, prostate cancer, ovarian cancer, breast cancer, pancreas cancer, cervix cancer, sarcomas and melanomas.

The present invention will be further explained with the following examples which are not limiting. As can be seen, this methodology allows for the synthesis of myriaporone compounds with the desired stereospecificity.

EXAMPLES

Example 1: Compound **7a**

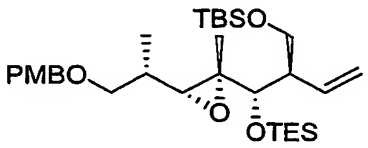


To a solution of **6** (3.51 g, 7.8 mmol) in CH_2Cl_2 (40 mL) was added imidazole (1.59 g, 23.4 mmol) and TBSCl (1.76 g, 11.7 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. HCl 0.1 N was added until pH= 4-5, and the mixture was extracted with CH_2Cl_2 (2x). The combined organic layers were dried over Na_2SO_4, filtered, and

concentrated under reduced pressure. The residue was purified by chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **7a** (3.44 g, 78%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 5.83 (m, 1H), 4.99 (dd, *J*= 10.5, 1.8 Hz, 1H), 4.86 (dd, *J*= 17.4, 2.1 Hz, 1H), 4.42 (s, 2H), 3.80 (s, 3H), 3.44 (m, 2H), 3.33 (d, *J*= 6.6 Hz, 1H), 2.47 (d, *J*= 9.6 Hz, 1H), 2.24 (m, 1H), 1.75 (m, 1H), 1.08 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.13 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 136.2, 130.3, 129.1, 117.1, 113.7, 72.9, 72.6, 64.9, 64.6, 63.9, 55.2, 51.3, 33.1, 25.9, 25.8, 18.2, 18.1, 14.9, 13.3, -4.2, -5.3, -5.4, -5.5. MS (ESI) m/z: 587 $(M+23)^+$.
$[\alpha]^{25}_D$ -9.5 (*c* 0.52, CH_2Cl_2).
R_f = 0.61 (Hex:EtOAc, 4:1).

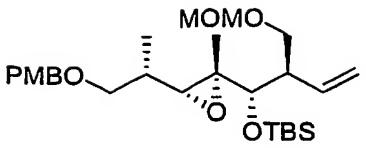
Example 2: Compound **7b**



Compound **7b** was prepared as a colourless oil, in the same way as **7b** from the corresponding precursor of **6**, according to the procedure described by W. Roush *et al.*, *Org. Lett.* **1999**, *1*, 95) by using TESOTf instead of TBSOTf in equivalent amounts for the secondary alcohol protection step.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 5.92-5.80 (m, 1H), 5.02 (dd, *J*= 10.2, 1.8 Hz, 1H), 4.90 (dd, *J*= 17.4, 1.8 Hz, 1H), 4.42 (s, 2H), 3.78 (s, 3H), 3.56-3.42 (m, 3H), 3.38-3.34 (m, 2H), 2.52 (d, *J*= 9.0 Hz, 1H), 2.27-2.23 (m, 1H), 1.81-1.76 (m, 1H), 1.27 (s, 3H), 1.10 (d, *J*= 6.6 Hz, 3H), 0.98 (t, *J*= 7.8 Hz, 9H), 0.90 (s, 9H), 0.71-0.62 (m, 6H), 0.05 (s, 3H), 0.04 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 136.4, 130.2, 129.0, 116.8, 113.6, 76.9, 72.8, 72.6, 64.7, 64.6, 63.8, 55.0, 51.1, 33.2, 25.7, 18.0, 14.8, 13.1, 6.9, 4.8, -5.3, -5.5.
MS (ESI) m/z: 587 $(M+23)^+$, 565 $(M+1)^+$.
R_f= 0.62 (Hexane:EtOAc, 4:1).

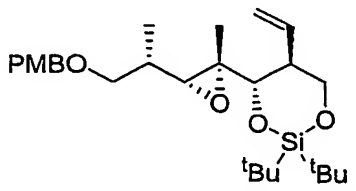
Example 3: Compound **7c**



To a solution of **6** (450 mg, 1 mmol) in CH_2Cl_2 (20 mL) was added DIPEA (1.74 mL, 10 mmol) and MOMBr (0.45 mL, 5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h. Then, a saturated aqueous solution of NH_4Cl was added and the mixture was extracted with CH_2Cl_2 (2x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **7c** (250 mg, 51%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 5.90-5.78 (m, 1H), 5.04 (dd, *J*= 10.2, 2.1 Hz, 1H), 4.95 (dd, *J*= 17.4, 2.1 Hz, 1H), 4.56 (s, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.51-3.40 (m, 1H), 3.37-3.34 (m, 4H), 3.33 (s, 3H), 2.52 (d, *J*= 9.3 Hz, 1H), 2.43-2.40 (m, 1H), 1.79-1.65 (m, 1H), 1.25 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.04 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 136.4, 130.6, 129.4, 117.6, 114.0, 96.8, 78.2, 73.1, 72.7, 69.0, 64.8, 64.7, 55.6, 55.5, 49.2, 33.4, 26.2, 18.5, 15.2, 13.5, -3.9, -5.3.
R_f = 0.52 (Hex:EtOAc, 4:1).

Example 4: Compound **7d**



To a solution of the corresponding diol (581 mg, 1.73 mmol) in CH_2Cl_2 (20 mL) was added 2,6-lutidine (0.61 g, 5.2 mmol) and t-$Bu_2Si(OTf)_2$ (9.48 mL mL, 2.6 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. Then, a saturated aqueous

solution of NH_4Cl was added and the mixture was extracted with CH_2Cl_2 (2x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **7d** (330 mg, 40%) as a colourless oil.

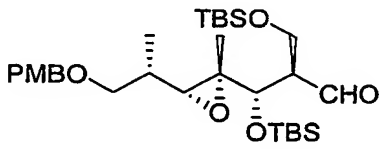
^1H NMR (300 MHz, $CDCl_3$) d 7.23 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 6.40 (ddd, *J*= 17.1, 9.9, 8.7 Hz, 1H), 5.10 (dd, *J*= 10.5, 1.8 Hz, 1H), 5.06 (dd, *J*= 17.1, 1.8 Hz, 1H), 4.41 (s, 2H), 4.35 (dd *J*= 11.1, 3.0 Hz, 1H), 4.06 (d, *J*= 3.0 Hz, 1H), 4.00 (dd, *J*= 11.1, 2.4 Hz, 1H), 3.80 (s, 3H), 3.34 (d, *J*= 6.3 Hz, 2H), 2.72 (d, *J*= 9.3 Hz, 1H), 2.41-2.37 (m, 1H), 1.78-1.73 (m, 1H), 1.28 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 3H), 1.07 (s, 9H), 1.05 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 136.9, 130.7, 129.2, 116.9, 114.0, 79.6, 73.1, 72.8, 70.4, 63.7, 62.3, 55.5, 47.0, 33.3, 28.6, 27.7, 23.5, 21.0, 15.1.

MS (ESI) m/z: 499 $(M+23)^+$.

R_f = 0.41 (Hex:EtOAc, 4:1).

Example 5: Compound **8a**



Over a solution of **7a** (21.94 g, 38.7 mmol) in CH_2Cl_2 (150 mL) was bubbled a current of O_3 during 50 min at -78 °C. Then, Ph_3P (30.45 g, 116.1 mmol) was added and the mixture was allowed to warm to room temperature, and the stirring was continued for 12 h. The mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to afford compound **8a** (15.82 g, 72%) as a colourless oil.

^1H NMR (300 MHz, $CDCl_3$) δ 9.67 (d, *J*= 3.0 Hz, 1H), 7.20 (d, *J*= 8.4 Hz, 2H), 6.84 (d, *J*= 8.4 Hz, 2H), 4.38 (m, 2H), 3.84 (dd, *J*= 10.2, 5.1 Hz, 1H), 3.80 (s, 3H), 3.69 (m, 2H), 3.41 (dd, *J*= 9.3, 5.1 Hz, 1H), 3.31 (t, *J*= 9.0 Hz, 1H), 2.59 (d, *J*= 9.3 Hz, 1H), 2.50 (m,

1H), 1.81 (m, 1H), 1.30 (s, 3H), 1.06 (d, *J*= 6.3 Hz, 3H), 0.86 (s, 18H), 0.14 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H).

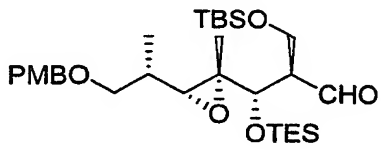
^{13}C NMR (75 MHz, $CDCl_3$) δ 203.8, 159.5, 130.3, 129.4, 114.0, 76.5, 73.2, 73.0, 65.1, 64.0, 60.1, 57.9, 55.4, 33.6, 26.0, 26.0, 18.3, 15.0, 13.0, -4.0, -5.2, -5.3, -5.5.

MS (ESI) m/z: 589 $(M+23)^+$.

$[\alpha]^{25}_D$ -11.6 (*c* 0.50, CH_2Cl_2).

R_f = 0.59 (Hex:EtOAc, 4:1).

Example 6: Compound **8b**



To a solution of **7b** (0.86 g, 1.52 mmol) in THF:H_2O (10:1, 22 mL) was added NMO (0.623 g, 5.32 mmol) and OsO_4 (4.56 mL, 0.456 mmol, 0.1 M in ^{t}BuOH) at 23 °C and the reaction mixture was stirred at 23 °C overnight. Florisil (6 g), $NaHSO_3$ (6 g), and EtOAc (100 mL) were added and the mixture was stirred vigorously during 30 min. The mixture was filtered through a pad of Celite, and the filtrate was concentrated to provide the corresponding diol. To a solution of this diol in THF (10 mL) was added a solution of $NaIO_4$ (1.95 g, 9.12 mmol) in H_2O (8 mL) at 0 °C and the mixture was stirred at 23 °C for 1 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (20 mL) and then, extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to afford compound **8b** (0.67 g, 78%) as a colourless oil.

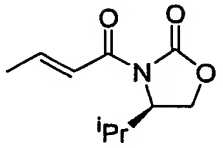
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (d, *J*= 2.4 Hz, 1H), 7.17 (d, *J*= 8.4 Hz, 2H), 6.83 (d, *J*= 8.4 Hz, 2H), 4.36 (q, *J*= 11.4 Hz, 2H), 3.83 (dd, *J*= 10.2, 5.1 Hz, 1H), 3.76 (s, 3H), 3.74 (d, *J*= 6.3 Hz, 1H), 3.67 (dd, *J*= 10.2, 5.7 Hz, 1H), 3.39 (dd, *J*= 9.3, 5.1 Hz, 1H), 3.30 (t, *J*= 9.0 Hz, 1H), 2.60 (d, *J*= 9.3 Hz, 1H), 2.47-2.40 (m, 1H), 1.82-1.78 (m, 1H), 1.28 (s, 3H), 1.04 (d, *J*= 6.6 Hz, 3H), 0.92 (t, *J*= 7.8Hz, 9H), 0.85 (s, 9H), 0.62 (q, *J*= 7.8 Hz, 6H), 0.01, (s, 3H), 0.00 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 159.1, 129.9, 129.0, 113.6, 75.9, 72.8, 72.6, 64.9, 63.5, 59.7, 57.4, 55.0, 33.3, 25.6, 17.9, 14.6, 12.5, 6.7, 4.6, -5.5, -5.7.

MS (ESI) m/z: 589 $(M+23)^+$.

R_f= 0.54 (Hexane:EtOAc, 4:1).

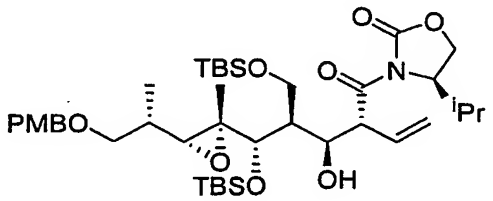
Example 7: Compound **9**



Compound **9** was prepared following the procedure described by D. A. Evans *et al.*, *J. Am. Chem. Soc.* **1984**, *106*, 4261-4263.

^1H NMR (300 MHz, $CDCl_3$) δ 7.21 (m, 1H), 7.12 (m, 1H), 4.44 (m, 1H), 4.20 (m, 2H), 2.36 (m, 1H), 1.91 (dd, *J*= 6.6, 1.2 Hz, 3H), 0.88 (d, *J*= 6.9 Hz, 3H), 0.83 (d, *J*= 6.9 Hz, 3H).

Example 8: Compound **10a**



To a solution of **9** (17.75 g, 0.09 mol) in CH_2Cl_2 (270 mL) was added Bu_2BOTf (99 mL, 1M in CH_2Cl_2, 0.099 mol) and Et_3N (17.56 mL, 0.126 mol) at -78 °C. The reaction mixture was stirred 1 h at -78 °C, 15 min at 0 °C and recooled at -78 °C. This solution was added in three portion in 5 h over a solution of **8a** (17.18 g, 0.03 mol) in CH_2Cl_2 (100 mL) at 0 °C and the mixture was stirred at -30°C for an additional 12 h. Then, saturated aqueous solution of NH_4Cl (300 mL) was added and the reaction was extracted with CH_2Cl_2 (2x 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved

in 400 mL of ether, 200 mL of buffer solution and 200 mL of H_2O_2 and the mixture was stirred at 0°C forl h. Then, the reaction was extracted and the organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (200 mL) and brine (200 mL). The organic layer were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 10:1 to 2:1) to afford compound **10a** (21 g, 92%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, *J*= 8.4 Hz, 2H), 6.85 (d, *J*= 8.4 Hz, 2H), 5.93 (m, 1H), 5.41 (d, *J*= 17.1 Hz, 1H), 5.28 (d, *J*= 9.3 Hz, 1H), 4.92 (t, *J*= 9.6 Hz, 1H), 4.63 (dddd, *J*= 9.3, 6.3, 5.1, 1.5 Hz, 1H), 4.43 (s, 3H), 4.34 (m, 1H), 4.12 (m, 2H), 3.85 (m, 1H), 3.80 (s, 3H), 3.73 (m, 2H), 4.44 (m, 2H), 2.58 (d, *J*= 9.3 Hz, 1H), 2.30 (m, 1H), 1.81 (m, 1H), 1.38 (s, 3H), 1.10 (d, *J*= 6.6 Hz, 3H), 0.93 (s, 9H), 0.87 (s, 9H), 0.84 (d, *J*= 7.5 Hz, 3H), 0.80 (d, *J*= 6.9 Hz, 3H), 0.17 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H).

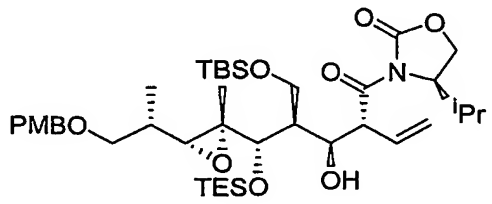
^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 159.0, 153.3, 135.3, 129.9, 128.6, 113.7, 77.4, 72.6, 71.0, 64.0, 63.4, 62.6, 59.8, 58.4, 58.0, 55.2, 51.2, 45.2, 40.1, 33.6, 26.7, 28.3, 27.8, 26.1, 25.8, 18.3, 17.9, 15.1, 14.6, 14.3, 13.1, -4.4, -5.4, -5.5, -5.6.

MS (ESI) m/z: 786 $(M+23)^+$.

$[\alpha]^{25}_D$ +3.1 (*c* 0.53, CH_2Cl_2).

R_f = 0.35 (Hex:EtOAc, 4:1).

Example 9: Compound **10b**



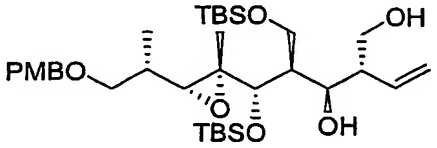
The title compound was prepared as described above from **8b** (1.2 g, 2.11 mmol). Chromatography (SiO_2,) provided **10b** (1.16 g, 80%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.4 Hz, 2H), 6.84 (d, *J*= 8.4 Hz, 2H), 5.85-6.03 (m, 1H), 5.19-5.44 (m, 2H), 4.93 (t, *J*= 9.3 Hz, 1H), 4.59-4.64 (m, 1H), 4.42-4.46

(m, 1H), 4.42 (s, 2H), 4.19-4.36 (m, 4H), 4.05-4.15 (m, 2H), 3.80 (s, 3H), 3.65-3.83 (m, 3H), 3.40-3.46 (m, 1H), 2.57 (d, J= 9.3 Hz, 1H), 2.27-2.36 (m, 1H), 1.78-1.86 (m, 1H), 1.56-1.64 (m, 1H), 1.37 (s, 3H), 1.28-1.38 (m, 6H), 0.92 (s, 9H), 0.88-0.99 (m, 6H), 0.62-0.68 (m, 9H), 0.09 (s, 3H), 0.04 (s, 3H).

R_f = 0.42 (Hex:EtOAc, 4:1).

Example 10: Compound **11a**



To a solution of **10a** (14.5 g, 18.9 mmol) in THF:H_2O (5:1, 120 mL), $LiBH_4$ (141.9 mL, 2.0 M in THF, 283.7 mmol,) was added at 0 °C. The reaction mixture was stirred 30 min at 0 °C and 6 h at 23 °C. Saturated aqueous solution of NH_4Cl (150 mL) was added and the mixture was extracted with EtOAc (3x150 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved in 400 mL of ether, 200 mL of buffer solution and 200 mL of H_2O_2 and the mixture was stirred at 0 °C for 2 h. Then, the reaction was extracted and the organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (2x200 mL). The organic layer were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc 5:1) to afford compound **11a** (10.5 g, 87%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J= 8.4 Hz, 2H), 6.87 (d, J= 8.4 Hz, 2H), 5.84 (m, 1H), 5.21 (d, J= 8.7 Hz, 1H), 5.14 (d, J= 17.4 Hz, 1H), 4.42 (s, 2H), 4.19 (m, 1H), 3.84 (m, 1H), 3.80 (s, 3H), 3.75 (m, 1H), 3.61 (m, 2H), 3.48 (m, 2H), 3.36 (m, 2H), 2.53 (d, J= 9.3 Hz, 1H), 2.27 (m, 1H), 1.80 (m, 1H), 1.32 (s, 3H), 1.05 (d, J= 6.9 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.15 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

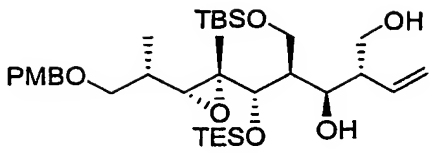
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 137.6, 130.3, 129.4, 118.3, 114.0, 73.2, 73.0, 71.2, 64.9, 64.4, 60.4, 55.5, 51.1, 47.0, 33.5, 29.9, 26.4, 26.3, 26.0, 18.4, 18.2, 15.0, 14.0, -4.2, -5.1, -5.2.

MS (ESI) m/z: 662 $(M+23)^+$.

$[\alpha]^{25}_D$ +0.7 (*c* 0.54, CH_2Cl_2).

R_f = 0.2 (Hex:EtOAc, 4:1).

Example 11: Compound **11b**



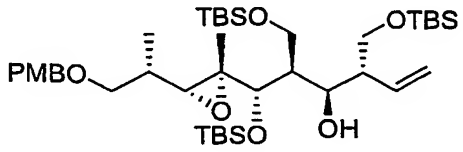
The title compound was prepared as described above from **10b** (1.53 g, 2 mmol). Chromatography (SiO_2,) provided **11b** (1 g, 80%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 5.92-5.80 (m, 1H), 5.92-5.80 (m, 1H), 5.21 (dd, *J*= 10.2, 2.1 Hz, 1H), 5.14 (dd, *J*= 17.1, 2.1 Hz, 1H), 4.40 (s, 2H), 4.19-4.16 (m, 1H), 3.84 (dd, *J*= 6.0, 1.5, 1H), 3.80 (s, 3H), 3.72 (dd, *J*= 6.3, 2.4 Hz, 1H), 3.62 (d, *J*= 4.5 Hz, 1H), 3.56 (d, *J*= 3.6, 1H), 3.52-3.48 (m, 1H), 3.38-3.33 (m, 2H), 2.53 (d, *J*= 9.0 Hz, 1H), 2.27-2.22 (m, 1H), 1.83-1.78 (m, 1H), 1.73-1.67 (m, 1H), 1.30 (s, 3H), 1.04 (d, *J*= 6.9 Hz, 3H), 0.95 (t, *J*= 7.8 Hz, 9H), 0.87 (s, 9H), 0.67 (q, *J*= 7.8 Hz, 6H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 137.4, 130.1, 129.1, 118.0, 113.7, 77.4, 72.9, 72.7, 71.1, 64.9, 64.3, 64.2, 60.2, 55.2, 51.0, 46.6, 33.3, 25.7, 17.9, 14.8, 13.5, 6.8, 4.7, -5.3, -5.5.

Rf = 0.18 (Hex:EtOAc 4:1).

Example 12: Compound **12a**



To a solution of **11a** (7.43 g, 11.6 mmol) in CH_2Cl_2 (100 mL) was added imidazole (3.16 g, 46.4 mmol) and TBSCl (3.48 g, 23.2 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 4 h. 0.1N HCl was added until pH= 4-5, and the reaction was

extracted with CH_2Cl_2 (2x150 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 10:1 to 4:1) to obtain compound **12a** (8.47 g, 97%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.6 Hz, 2H), 6.86 (d, *J*= 8.6 Hz, 2H), 5.86 (m, 1H), 5.07 (m, 2H), 4.41 (m, 2H), 4.29 (br s, 1H), 3.88 (m, 1H), 3.80 (s, 3H), 3.74 (m, 1H), 3.62 (m, 2H), 3.48 (m, 1H), 3.34 (d, *J*= 6.8 Hz, 2H), 3.17 (d, *J*= 4.9 Hz, 1H), 2.55 (d, *J*= 9.2 Hz, 1H), 2.26 (m, 1H), 1.78 (m, 2H), 1.32 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.16 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H), 0.03 (s, 9H).

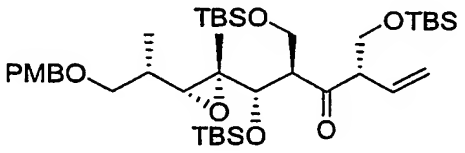
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 138.0, 130.5, 129.2, 117.1, 114.0, 77.4, 73.1, 72.8, 69.4, 65.0, 64.8, 64.5, 60.7, 55.4, 51.9, 46.9, 33.7, 29.9, 26.3, 26.2, 26.1, 18.6, 18.5, 18.1, 15.1, 13.5, -4.3, -5.0, -5.1, -5.2.

MS (ESI) m/z: 775 $(M+23)^+$, 753 $(M+1)^+$.

$[\alpha]^{25}_D$ +3.0 (*c* 0.54, CH_2Cl_2).

R_f = 0.66 (Hex:EtOAc, 4:1).

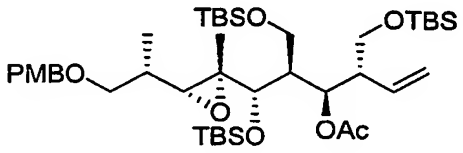
Example 13: Compound **12b**



To a solution of **12a** (500 mg, 0.663 mmol) in CH_2Cl_2 (30 mL) was added Dess-Martin periodinane (562 mg, 1.32 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. Then, saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **12b** (414 mg, 83%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 5.78 (m, 1H), 5.23 (m, 2H), 4.42 (dd, *J*= 16.2, 11.4, 2H), 4.02 (dd, *J*= 10.2, 4.8 Hz, 1H), 3.81 (s, 3H), 3.74 (m, 1H), 3.61 (m, 2H), 3.33 (m, 3H), 2.48 (d, *J*= 9.3 Hz, 1H), 1.77 (m, 1H), 1.29 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.84 (s, 9H), 0.11 (s, 3H), 0.04 (s, 3H), 0.03, (s, 3H), 0.02, (s, 3H), -0.01, (s, 3H), -0.03 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 159.1, 134.3, 130.2, 129.0, 119.3, 113.7, 77.5, 72.7, 72.2, 64.3, 63.0, 62.3, 62.2, 61.1, 55.9, 55.2, 33.6, 29.7, 26.0, 25.9, 25.8, 18.2, 18.1, 15.0, 12.2, -4.5, -5.2, -5.3, -5.4, -5.4, -5.5.
MS (ESI) m/z: 773 $(M+23)^+$.

Example 14: Compound **12c**

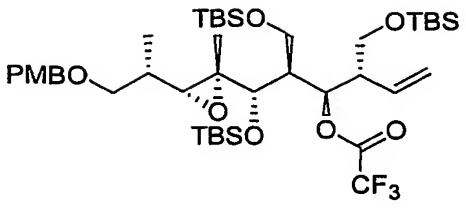


To a solution of **12a** (1.5 g, 1.99 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (5.55 mL, 39.82 mmol), DMAP (24 mg, 0.119 mmol) and Ac_2O (1.88 mL, 19.91 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 12 h. Then, a saturated aqueous solution of $NaHCO_3$ (50 mL) was added and and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were washed with HCl 0.1 N, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **12c** (1.12 g, 71%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.5 Hz, 2H), 6.86 (d, *J*= 8.5 Hz, 2H), 5.66 (m, 1H), 5.48 (m, 2H), 5.09 (m, 2H), 4.42 (m, 2H), 3.80 (s, 3H), 3.60 (m, 2H), 3.46 (m, 2H), 3.34 (m, 4H), 2.61 (m, 1H), 2.48 (d, *J*= 9.1 Hz, 1H), 1.95 (s, 3H), 1.77 (m, 1H), 1.34 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H), 0.03 (s, 6H), 0.01 (s, 3H), -0.01 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 159.4, 136.7, 130.6, 129.3, 118.3, 114.0, 76.9, 73.0, 72.6, 70.6, 64.4, 59.9, 55.4, 52.5, 47.1, 33.4, 26.3, 26.1, 26.1, 21.4, 18.6, 18.3, 15.2, 13.3, -4.1, -4.9, -5.0, -5.1, -5.2, -5.2.
MS (ESI) m/z: 817 $(M+23)^+$, 812 $(M+18)^+$.

R_f = 0.63 (Hex:EtOAc, 4:1).

Example 15: Compound **12d**



To a solution of **12a** (215 mg, 0.285 mmol) in THF (5 mL) was added Py (0.46 mL, 5.7 mmol), DMAP (53 mg, 0.427 mmol) and $(CF_3CO)_2O$ (0.40 mL, 2.85 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 12 h. Then, a saturated aqueous solution of $NaHCO_3$ (7 mL) was added and the reaction was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were washed with HCl 0.1N (2x4 mL),dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 18:1) to obtain compound **12d** (221 mg, 91%) as a colourless oil.

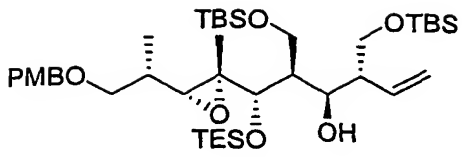
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 5.75 (m, 1H), 5.65 (m, 1H), 5.09 (m, 2H), 4.42 (s, 2H), 3.81 (s, 3H), 3.47 (m, 8H), 2.78 (m, 1H), 2.51 (d, *J*= 9.0 Hz, 1H), 2.11 (m, 1H), 1.78 (m, 1H), 1.33 (s, 3H), 1.06 (d, *J*= 6.9 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 18H), 0.12 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.01 (s, 6H), 0.00 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 156.0 (d, J_{C-F}= 41.0 Hz), 134.6, 130.2, 129.1, 119.4, 113.8, 76.0, 75.4, 72.9, 72.7, 64.3, 64.0, 63.8, 59.3, 55.2, 51.6, 46.2, 33.1, 26.1, 25.9,18.3, 18.0, 14.8, 14.1, 13.2, -4.5, -5.0, -5.4, -5.5, -5.6, -5.7.

MS (ESI) m/z: 866 $(M+18)^+$.

R_f = 0.45 (Hex:EtOAc, 4:1).

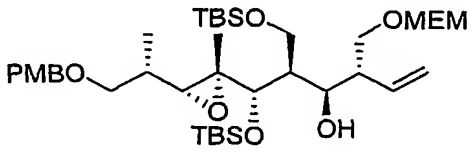
Example 16: Compound **12e**



The title compound was prepared as described above in example 12, starting from **11b** (0.7 g, 1.09 mmol). Chromatography (SiO_2, Hex:EtOAc, 15:1) provided **12e** (661 g, 80%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 5.95-5.82 (m, 1H), 5.13-5.03 (m, 2H), 4.41(dd, *J*= 15.6, 11.7 Hz, 2H), 4.30-4.26 (m 1H), 3.86 (dd, *J*= 13.8, 3.6 Hz, 1H), 3.79 (s, 3H), 3.74 (dd, *J*= 10.5, 6.3 Hz, 1H), 3.64 (d, *J*= 5.7 Hz, 1H), 3.61 (d, *J*= 6.3 Hz, 1H), 3.50 (dd, *J*= 9.9, 5.1 Hz, 1H), 3.34 (d, *J*= 7.5 Hz, 2H), 3.18 (d, *J*= 4.8 Hz, 1H), 2.56 (d, *J*= 9.0 Hz, 1H), 2.32-2.23 (m, 1H), 1.85-1.79 (m 1H), 1.74-1.71 (m, 1H), 1.31 (s, 3H), 1.06 (d, *J*= 6.9 Hz, 3H), 0.97 (t, *J*= 7.5 Hz, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.68 (q, 7.2, 6H), 0.05 (s, 3H), 0.04 (s, 6H), 0.03 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 137.6, 130.0, 128.8, 116.6, 113.5, 77.0, 72.6, 72.4, 69.1, 64.7, 64.6, 64.0, 60.2, 54.9, 51.3 46.2, 33.3, 25.7, 25.6, 18.0, 17.7, 14.7, 12.9, 6.7, 4.5, -5.5, -5.7.
MS (ESI) m/z: 775 $(M+23)^+$, 773 $(M+1)^+$.
R_f = 0.6 (Hex:EtOAc, 4:1).

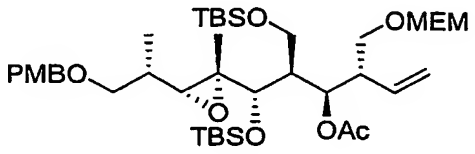
Example 17: Compound **12f**



To a solution of **11a** (500 mg, 0.78 mmol) in CH_2Cl_2 (10 mL) was added DIPEA (327 μL, 1.87 mmol) and MEMCl (107 μL, 0.94 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 14 h. Then, the reaction was extracted with HCl 0.1N (10 mL) and the organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc 10:1) to obtain compound **12f** (445 mg, 78%) as a colourless oil.

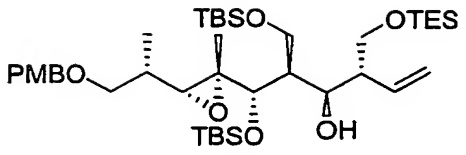
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 z, 2H), 5.92-5.79 (m, 1H), 5.16-5.09 (m, 2H), 4.67 (s, 2H), 4.42 (dd, *J*= 15.3, 11.7 Hz, 2H), 4.23-4.18 (m, 1H), 4.85 (dd, *J*= 10.5, 4.8 Hz, 1H), 3.80 (s, 3H), 3.67-3.64 (m, 2H), 3.60 (d, *J*= 5.7 Hz, 2H), 3.57-3.51 (m, 2H), 3.49-3.40 (m, 2H), 3.37 (3, 3H), 2.56 (d, *J*= 9.3 Hz, 1H), 2.45-2.40 (m, 1H), 1.85-1.77 (m, 1H), 1.74-1.72 (m, 1H), 1.30 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.15 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).
MS (ESI) m/z: 749 $(M+23)^+$.
R_f = 0.25 (Hex:EtOAc, 4:1).

Example 18: Compound **12g**



To a solution of **12f** (438 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (1.67 mL, 12 mmol), DMAP (74 mg, 0.6 mmol) and Ac_2O (567 μL, 6 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 12 h. Then, the reaction was extracted with HCl 0.1N (10 mL) and the organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc 7:1) to obtain compound **12g** (343 mg, 74%) as a colourless oil.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.1 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 5.74 (dt, *J*= 19.8, 9.9 Hz, 1H), 5.52-5.49 (m, 1H), 5.13-5.07 (m, 2H), 4.65 (s, 2H), 4.42 (dd, *J*= 13.5, 12.0 Hz, 2H), 3.80 (s, 3H), 3.66-3.62 (m, 2H), 3.60-3.57 (m, 1H), 3.54-3.47 (m, 4H), 3.40-3.34 (m, 1H), 3.38 (s, 3H), 3.28 (d, *J*= 5.7 Hz, 1H), 2.81-2.76 (m, 1H), 2.48 (d, *J*= 8.7 Hz, 1H), 1.97 (s, 3H), 1.83-1.73 (m, 1H), 1.56 (bs, 1H), 1.31 (s, 3H), 1.07 (d, *J*= 6.9 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.12 (s,3H), 0.06 (s, 3H), 0.03 (s, 6H).
MS (ESI) m/z: 791 $(M+23)^+$.
R_f = 0.26 (Hex:EtOAc, 4:1).

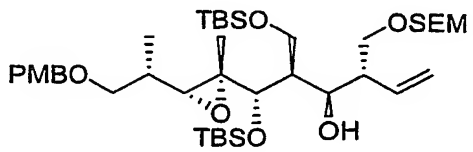
Example 19: Compound **12h**



To a solution of **11a** (75 mg, 0.117 mmol) in CH_2Cl_2 (3 mL) was added DIPEA (82 μL, 0.47 mmol) and TESCl (40 μL, 0.234 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 3 h. Then, 0.1N HCl was added until pH= 4-5, and the reaction was extracted with CH_2Cl_2 (2x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 12:1) to obtain compound **12h** (77 mg, 87%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 5.94-5.82 (m, 1H), 5.11 (dd, *J*= 9.9, 2.1 Hz, 1H), 5.08 (dd, *J*= 16.8, 2.1 Hz, 1H), 4.41(dd, *J*= 17.1, 11.7 Hz, 2H), 4.33-4.29 (m, 1H), 3.87 (dd,,1H), 3.80 (s, 3H), 3.65-3.60 (m, 2H), 3.49 (dd, *J*= 9.9, 5.1 Hz, 1H), 3.33 (d, *J*= 6.9 Hz, 2H), 3.24 (d, *J*= 4.5 Hz, 1H), 2.56 (d, *J*= 9.3 Hz, 1H), 2.30-2.25 (m, 1H), 1.82-1.75 (m, 2H), 1.31 (s, 3H), 1.03 (d, *J*= 6.6 Hz, 3H), 0.93-0.90 (m, 9H), 0.92 (s, 9H), 0.87 (s, 9H), 0.57 (q, *J*= 7.8 Hz, 6H), 0.16 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H).
MS (ESI) m/z: 775 $(M+23)^+$.
R_f = 0.58 (Hex:EtOAc, 4:1).

Example 20: Compound **12i**

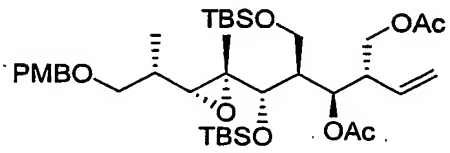


To a solution of **11a** (128 mg, 0.2 mmol) in CH_2Cl_2 (10 mL) was added DIPEA (104 μL, 0.6 mmol), DMAP (2 mg, 0.02 mmol) and SEMCl (53 μL, 0.3 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 6 h. Then, 0.1N HCl was added until pH=

4-5, and the reaction was extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **12i** (142 mg, 92%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.5 Hz, 2H), 6,86 (d, *J*= 8.5 Hz, 2H), 5.79-5.88 (m, 1H), 5.10-5.17 (m, 2H), 4.61 (s, 2H), 4.42 (dd, *J*= 15.9, 11.5 Hz, 2H), 4.17-4.22 (m, 1H), 3.76-3.87 (m, 1H), 3.79 (s, 3H), 3.42-3.62 (m, 3H), 3.36 (d, *J*= 6.8 Hz, 1H), 2.56 (d, *J*= 9.3 Hz, 1H), 2.40-2.45 (m, 1H), 1.72-1.83 (m, 2H), 1.25 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.15 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.00 (s, 9H).
^{13}C-NMR (75 MHz, CDCl3): d 159.4, 137.8, 130.4, 129.3, 117.4, 114.0, 95.2, 73.1, 72.8, 70.3, 69.4, 65.3, 64.8, 64.2, 60.6, 55.4, 49.2, 47.0, 33.8, 29.9, 26.3, 26.0, 18.5, 18.3, 18.1, 15.1, 13.7, -1.2, -4.2, -5.1, -5.2.
MS (ESI) m/z: 792 $(M+23)^+$.
R_f = 0.56 (Hex:EtOAc, 4:1).

Example 21: Compound **12j**



To a solution of **11a** (600 mg, 0.93 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (2.61 mL, 18.76 mmol), DMAP (115 mg, 0.93 mmol) and Ac_2O (887 μL, 9.39 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 3 h. Then, 0.1N HCl was added until pH= 4-5, and the reaction was extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 10:1 to 5:1) to obtain compound **12j** (592 mg, 87%) as a pale yellow oil.

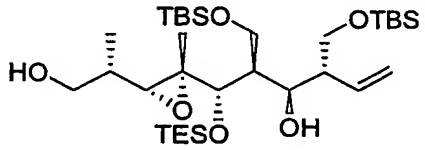
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 5.72-5.60 (m, 1H), 5.53-5.50 (m, 1H), 5.16-5.07 (m, 2H), 4.42 (s, 2H), 4.03 (dd, *J*= 11.1, 6.3

Hz, 1H), 3.90 (dd, *J*= 11.1, 6.9 Hz, 1H), 3.80 (s, 3H), 3.58 (dd, *J*= 10.2, 5.7 Hz, 1H), 3.47 (dd, *J*= 10.2, 6.3 Hz, 1H), 3.38-3.34 (m, 3H), 2.88-2.83 (m, 1H), 2.48 (d, *J*= 9.3 Hz, 1H), 2.01 (s, 3H), 1.98 (s, 3H), 1.95-1.90 (m, 1H), 1.83-1.74 (m, 1H), 1.32 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.12 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

MS (ESI) m/z: 745 $(M+23)^+$.

R_f = 0.34 (Hex:EtOAc, 4:1).

Example 22: Compound **12k**



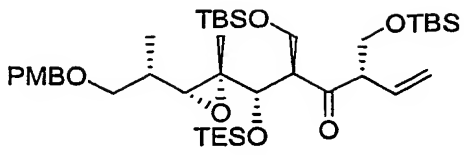
To a solution of crude **12e** (545 mg, 0.73 mmol) in a mixture of CH_2Cl_2:H_2O (8:0.4 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (329 mg, 1.45 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 45 min. Saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was solved in MeOH and $NaBH_4$ (70 mg, 1.9 mmol) was added. The mixture was stirred at 23 °C for 2 h and then, the reaction was concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain **12k** (300 mg, 65%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88-5.80 (m, 1H), 5.15-5.09 (m, 2H), 4.18.4.17 (m, 1H), 3.92 (dd, *J*= 10.5, 4.5 Hz, 1H), 3.86-3.68 (m, 1H), 3.66-3.56 (m, 3H), 3.50-3.47 (m, 1H), 3.33 (d, *J*= 3.9, 1H), 2.54 (d, *J*= 9.3 Hz, 1H), 2.38-2.34 (m, 1H), 1.87-1.86 (m, 1H), 1.71-1.62 (m, 1H), 1.33 (s, 3H), 1.03 (d, *J*= 6.9 Hz, 3H), 0.95 (t, *J*= 8.1 Hz, 9H), 0.87 (s, 9H), 0.87 (s, 9H), 0.67 (q, *J*= 8.4 Hz, 6H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

MS (ESI) m/z: 655 $(M+23)^+$, 633 $(M+1)^+$.

R_f = 0.38 (Hex:EtOAc, 4:1).

Example 23: Compound **12l**



To a solution of **12e** (100 mg, 0.13 mmol) in CH_2Cl_2 (6 mL) was added Dess-Martin periodinane (113 mg, 0.26 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 2 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to obtain **12l** (110 mg, 96 %) as a pale yellow oil.

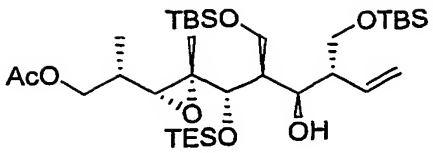
^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J*= 8.7 Hz, 2H), 6.90 (d, *J*= 8.7 Hz, 2H), 5.78 (ddd, *J*= 16.8, 10.2, 9.0 Hz, 1H), 5.29-5.22 (m, 2H), 4.43 (q, *J*= 11.4 Hz, 2H), 4.04 (dd, *J*= 10.2, 4.2 Hz, 1H), 3.84 (s, 3H), 3.77-3.72 (m, 1H), 3.66-3.60 (m, 2H), 3.45-3.30 (m, 5H), 2.50 (d, *J*= 9.3 Hz, 1H), 1.85-1.75 (m, 1H), 1.32 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 1H), 0.95 (t, *J*= 7.8 Hz, 9H), 0.91 (s, 9H), 0.87 (s, 9H), 0.63 (q, *J*= 7.8 Hz, 6H), 0.08 (s, 3H), 0.07 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 209.9, 159.1, 134.3, 130.2, 129.0, 119.3, 113.7, 78.0, 72.3, 72.1, 64.8, 63.0, 62.6, 62.3, 61.1, 56.1, 55.2, 33.6, 29.7, 25.9, 25.8, 18.2, 18.1, 15.1, 11.9, 6.8, 4.6, -5.3, -5.4, -5.5.

MS (ESI) m/z: 773 $(M+23)^+$.

R_f = 0.57 (Hex:EtOAc, 4:1).

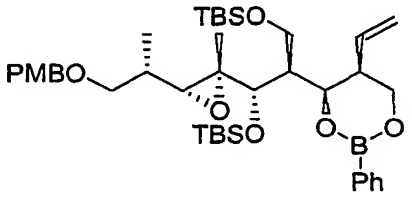
Example 24: Compound **12m**



To a solution of **12k** (280 mg, 0.44 mmol) in THF (5 mL) was added E_3N (368 μL, 2.64 mmol), DMAP (5 mg, 0.04 mmol) and Ac_2O (125 μL, 1.32 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 1 h. Then, 0.1N HCl was added until pH= 4-5, and the reaction was extracted with CH_2Cl_2 (2x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 15:1) to obtain compound **12m** (258 mg, 87%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90 (ddd, *J*= 17.1, 10.8, 9.6 Hz, 1H), 5.16-5.09 (m, 2H), 4.32-4.28 (m, 1H), 4.09 (dd, *J*= 11.1, 5.7 Hz, 1H), 3.89-3.76 (m, 3H), 3.70-3.67 (m, 2H), 3.56 (dd, *J*= 9.9, 5.1 Hz, 1H), 3.08, (d, *J*= 4.5 Hz, 1H), 2.57 (d, *J*= 9.3 Hz, 1H), 2.40-2.31 (m, 1H), 2.05 (s, 3H), 1.30 (s, 3H), 1.10 (d, *J*= 6.9 Hz, 3H), 0.96 (t, *J*= 8.1 Hz, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.69 (q, *J*= 8.1 Hz, 6H), 0.05 (s, 3H), 0.03 (s, 6H), 0.02 (s, 3H).
R_f = 0.66 (Hex:EtOAc, 4:1).

Example 25: Compound **12n**

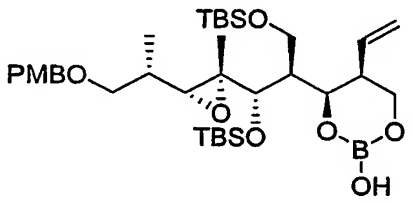


To a solution of **11a** (110 mg, 0.17 mmol) in CH_2Cl_2 (5 mL) was added $PhB(OH)_2$ (33 mg, 0.26 mmol) and the reaction mixture was stirred at 23 °C for 1 h. Then, the solution was filtered through a pad of celite. The filtrate was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 20:1 to 10:1) to obtain compound **12n** (94 mg, 75%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, *J*= 7.8, 1.2 Hz, 2H), 7.65-7.60 (m, 1H), 7.56-7.42 (m, 2H), 7.24 (d, *J*= 8.7 Hz, 2H), 6.83 (d, *J*= 8.7 Hz, 2 Hz), 5.88 (ddd, *J*= 18.9, 10.2, 8.7 Hz, 1H), 5.23-5.17 (m, 2 H), 4.54 (dd, *J*= 6.6, 2.4 Hz, 1H), 4.39 (dd, *J*= 18.0, 11.1 Hz, 2H), 4.27 (dd, *J*= 11.1, 3.3 Hz, 1H), 4.03 (brd, *J*= 0.5 Hz, 1H), 3.97 (dd, *J*= 10.2, 6.3 Hz, 1H), 3.82 (d, *J*= 5.1 Hz, 1H), 3.68 (s, 3H), 3.65 (dd, *J*= 10.5, 3.6 Hz, 1H), 3.46-3.35 (m, 2H), 2.87 (brd, *J*= 8.4 Hz, 1H), 2.70 (d, *J*= 9.3 Hz, 1H), 1.93-1.83 (m, 2H), 1.30 (s, 3H), 1.11 (d, *J*= 6.6 Hz, 3H), 0.95 (s, 9H), 0.92 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H), 0.08 (s, 3H), 0,07 (s, 3H).

R_f = 0.46 (Hex:EtOAc, 4:1).

Example 26: Compound **12o**



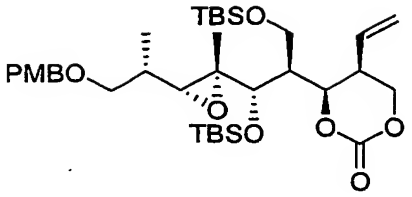
The title compound was obtained as precursor of **11a** in the reduction reaction of **10a** before the treatment with H_2O_2.^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.4 Hz, 2H), 6.85 (d, *J*= 8.4 Hz, 2H), 5.87-5.79 (m, 1H), 5.22-5.17 (m, 2H), 4.38 (dd, *J*= 10.8 Hz, 13.2 Hz, 2H), 4.30 (dd *J*= 6.6, 2.7 Hz, 1H), 4.07 (dd, *J*= 10.8, 3.0 Hz, 1H), 3.83-3.72 (m, 2H), 3.80 (s, 3H), 3.69 (d, *J*= 5.1 Hz, 1H), 3.50 (dd, *J*= 9.9, 3.0 Hz, 1H), 3.37-3.32 (m, 2H), 2.67 (brd, *J*= 8.4 Hz, 1H), 2.62 (d, *J*= 9.3 Hz, 1H), 1.81-1.76 (m, 2H), 1.21 (s, 3H), 1.06 (d, *J*= 6.9 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 134.0, 130.2, 129.1, 118.4, 113.7, 76.2, 72.9, 70.0, 67.1, 64.8, 59.5, 55.2, 45.7, 43.9, 33.4, 26.4, 26.0, 25.9, 25.5, 18.2, 14.9, 14.0, 13.3, -4.3, -4.9, -5.3, -5.4.

MS (ESI) m/z: 661 $(M+23)^+$.

R_f = 0.50 (Hex:EtOAc, 4:1).

Example 27: Compound **12p**



To a solution of **11a** (119 mg, 0.18 mmol) in THF (10 mL) was added CDI (49 mg, 0.3 mmol) and NaH (8 mg, 0.2 mmol) and the reaction mixture was stirred at 23 °C for 3 h. Then, a saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 5:1) to obtain **12p** (97 mg, 78%) as a pale yellow oil.

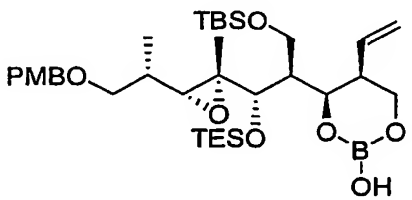
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 5.79-5.70 (m, 1H), 5.32-5.26 (m, 2H), 4.67 (dd, *J*= 7.5, 2.4 Hz, 1H), 4.43 (dd, *J*= 10.5, 3.6 Hz, 1H), 4.35 (q, *J*= 10.2 Hz, 2H), 4.25 (dd, *J*= 16.2, 15.3 Hz, 2H), 3.80 (s, 3H), 3.77-3.69 (m, 2H), 3.54 (dd, *J*= 10.5, 3.0 Hz, 1H), 3.42 (dd, *J*= 9.3, 4.8 Hz, 1H), 3.30 (t, *J*= 9.3 Hz, 1H), 2.92 (br d, *J*= 8.4 Hz, 1H), 2.66 (d, *J*= 9.6 Hz, 1H), 1.95-1.92 (m, 1H), 1.21 (s, 3H), 1.05 (d, *J*= 6.9 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.07 (s, 6H), 0.05 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 159.4, 154.1, 130.5, 129.4, 114.0, 99.3, 76.5, 73.0, 72.6, 68.0, 66.0, 64.7, 64.6, 63.6, 61.2, 59.5, 58.8, 55.4, 44.5, 42.1, 41.6, 33.7, 29.7, 28.8, 26.3, 26.3, 26.2, 26.1, 19.0, 18.6, 18.3, 18.2, 15.2, 14.9, 13.7, -4.1, -4.2, -5.1, -5.2.

MS (ESI) m/z: 687 $(M+23)^+$.

R_f = 0.47 (Hex:EtOAc, 4:1).

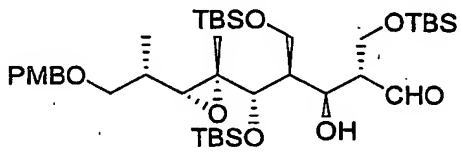
Example 28: Compound **12q**



The title compound was obtained as precursor of **11b** in the reduction reaction of **10b** before the treatment with H_2O_2. ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (d, *J*= 8.4 Hz, 2H), 6.82 (d, *J*= 8.7 Hz, 2H), 5.86-5.74 (m, 1H), 5.20-5.15 (m, 2H), 4.40-4.34 (m, 2H), 4.18-4.15 (m, 1H), 4.09-4.03 (m, 1H), 3.85-3.79 (m, 1H), 3.76 (s, 3H), 3.66 (d, *J*= 7.8 Hz, 1H), 3.58 (q, *J*= 7.2 Hz, 1H), 3.47 (dd, *J*= 9.9, 2.4 Hz, 1 H), 3.37-3.27 (m, 1H), 2.87 (br d, *J*= 8.7 Hz, 1H), 2.74 (q, *J*= 7.5 Hz, 1H), 2.63 (d, *J*= 9.3 Hz, 1H), 1.72-1.65 (m, 2H), 1.18 (s, 3H), 1.03 (d, *J*= 6.3 Hz, 3H), 0.91-0.85 (m, 9H), 0.84 (s, 9H), 0.60 (q, *J*= 7.8Hz, 6H), -0.01 (s, 3H), -0.02 (s, 3H).

R_f = 0.65 (Hex:EtOAc, 4:1).

Example 29: Compound **13a**



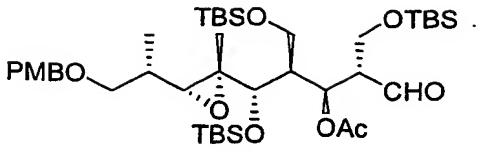
Over a solution of **12a** (5.91 g, 7.85 mmol) in CH_2Cl_2 (80 mL) was bubbled a current of O_3 during 15 min at -78 °C. Then, Ph_3P (6.29 g, 24 mmol) was added and the mixture was allowed to warm to room temperature, and the stirring was continued for 12 h. The mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to afford compound **13a** (4.99 g, 84%) as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (d, *J*= 3.0 Hz, 1H), 7.20 (d, *J*= 8.7 Hz, 2H), 6.85 (d, *J*= 8.7 Hz, 2H), 4.66 (m, 1H), .439 (s, 2H), 3.84 (m, 2H), 3.78 (s, 3H), 3.68 (m, 2H), 3.61 (m, 2H), 3.37 (m, 2H), 2.58 (d, *J*= 9.0 Hz, 1H), 2.44 (m, 1H), 1.82 (m, 1H), 1.72 (m, 1H), 1.29 (s, 3H), 1.05 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H), 0.06 (s, 6H), 0.00 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 159.2, 130.0, 129.0, 113.7, 76.4, 72.8, 72.7, 67.9, 64.6, 63.9, 60.8, 60.1, 57.7, 55.1, 44.4, 33.5, 26.1, 25.7, 18.3, 18.1, 17.8, 14.8, 12.9, -4.6, -5.3, -5.5, -5.5, -5.7, -5.7.

$[\alpha]^{25}_D$ +2.3 (*c* 0.50, CH_2Cl_2).

R_f = 0.46 (Hex:EtOAc, 4:1).

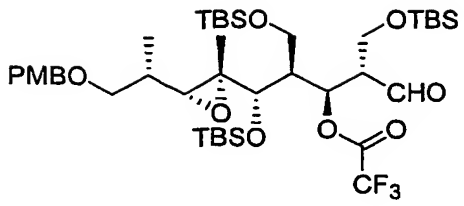
Example 30: Compound **13b**



To a solution of **12c** (2.25 g, 2.84 mmol) in THF:H_2O (70:30, 105 mL) was added NMO (1.16 g, 9.94 mmol) and OsO_4 (5.68 mL, 0.568 mmol, 0.1 M in ^tBuOH) at 23 °C and the reaction mixture was stirred at 23 °C overnight. Florisil (16 g), $NaHSO_3$ (16 g), and EtOAc (160 mL) were added and the mixture was stirred vigorously during 30 min. The mixture was filtered through a pad of Celite, and the filtrate was concentrated to provide the corresponding diol. This diol was dissolved in anhydrous Toluene (50 mL) and $Pb(OAc)_4$ (1.57 g, 3.55 mmol) was added at 0 °C, stirred for 30 min, filtered through a pad of Celite, washed with EtOAc and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to afford compound **13b** (0.97 g, 43%) as a colourless oil.

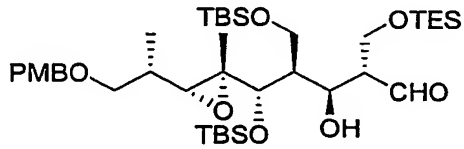
^1H NMR (300 MHz, $CDCl_3$) δ 9.61 (d, *J*= 3.9 Hz, 1H), 7.22 (d, *J*= 8.5 Hz, 2H), 6.87 (d, *J*= 8.5 Hz, 2H), 5.56 (dd, *J*= 10.3, 6.6 Hz, 1H), 4.42 (s, 2H), 3.95 (m, 1H), 3.80 (s, 3H), 3.54 (m, 2H), 3.38 (d, *J*= 7.0 Hz, 2H), 3.24 (d, *J*= 6.8 Hz, 1H), 3.04 (m, 1H), 2.49 (d, *J*= 9.0 Hz, 1H), 1.98 (s, 3H), 1.79 (m, 1H), 1.31 (s, 3H), 1.06 (d, *J*= 6.8 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.06 (s, 6H), 0.04 (s, 3H), 0.03 (s, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 203.3, 170.1, 159.4, 130.4, 129.3, 114.0, 76.6, 73.1, 72.7, 69.1, 64.4, 63.9, 61.3, 60.0, 58.4, 55.4, 46.4, 33.4, 29.9, 26.4, 26.1, 26.0, 21.2, 18.6, 18.4, .18.3, 15.1, 12.8, -4.1, -5.0, -5.1, -5.2, -5.3, -5.4.
MS (ESI) m/z: 819 $(M+23)^+$.
R_f = 0.47 (Hex:EtOAc, 4:1).

Example 31: Compound **13c**



To a solution of **13a** (90 mg, 0.12 mmol) in CH_2Cl_2 (10 mL) was added Py (0.19 mL, 2.4 mmol), DMAP (22 mg, 0.18 mmol) and $(CF_3CO)_2O$ (0.17 mL, 1.2 mmol) at 0 °C and the reaction mixture was stirred at 0 °C for 2 h. Then, the reaction was concentrated under reduced pressure to obtain **13c** which was used in subsequent steps with no further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.63 (d, *J*= 2.4 Hz, 1H), 7.19 (d, *J*= 8.6 Hz, 2H), 6.85 (d, *J*= 8.6 Hz, 2H), 5.75-5.79 (m, 1H), 4.34-4.42 (m, 2H), 3.86-3.90 (m, 2H), 3.78 (s, 3H), 3.48 (d, *J* = 5.4 Hz, 1H), 3.30-3.38 (m, 3H), 3.08-3.13 (m, 1H), 2.51 (d, *J*= 9.0 Hz, 1H), 2.21-2.27 (m, 1H), 1.77-1.82 (m, 1H), 1.25 (s, 3H), 1.05 (d, *J*= 6.8 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.02 (s, 6H), 0.00 (s, 3H).
R_f = 0.70 (Hex:EtOAc, 4:1).

Example 32: Compound **13d**



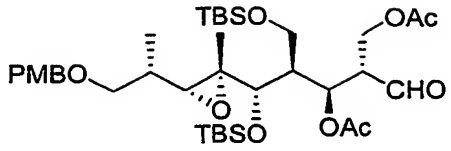
Following the procedure described in example 29, **12h** (1 g, 1.32 mol) was converted to **13d** (715 mg, 72%, colourless oil) after purification of the crude product by flash column chromatography (Hex:EtOAc, 20:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.81 (d, *J*= 3.0 Hz, 1H), 7.21 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.4 Hz, 2H), 4.70-4.64 (m, 1H), 4.40 (s, 2H), 3.89-3.81 (m, 1H), 3.80 (s, 3H), 3.75-3.66 (m, 2H), 3.64 (d, *J*= 6.6 Hz, 2H), 3.38-3.35 (m, 2H), 2.60 (d, *J*= 9.3 Hz, 1H), 2.50-2.46 (m, 1H), 1.85-1.80 (m, 1H), 1.77-1.68 (m, 1H), 1.29 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.94-087 (m, 9H), 0.92 (s, 9H), 0.87 (s, 9H), 0.55 (q, *J*= 7.8 Hz, 6H), 0.16 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H).

MS (ESI) m/z: 777 $(M+23)^+$.

R_f = 0.5 (Hex:EtOAc, 4:1).

Example 33: Compound **13e**

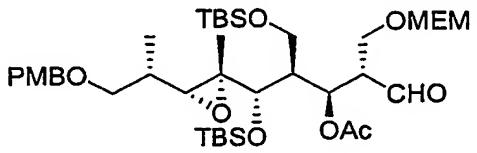


Following the procedure described in example 29, **12j** (590 mg, 0.81 mol) was converted to **13e** (420 mg, 71%, pale yellow oil) after purification of the crude product by flash column chromatography (Hex:EtOAc, 10:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.58 (d, *J*= 20.0 Hz, 1H), 7.19 (d, *J*= 8.4 Hz, 2H), 6.82 (d, *J*= 8.4 Hz, 2H), 5.58 (dd, *J*= 5.1, 4.6 Hz, 1H), 4.38 (s, 2H), 4.30-4.23 (m, 2H), 3.76 (s, 3H), 3.50 (dd, *J*= 6.9, 5.1 Hz, 2H), 3.30 (d, *J*= 7.0 Hz, 2H), 3.25-3.22 (m, 2H), 2.44 (d, *J*= 9.3 Hz, 1H), 2.15-2.12 (m, 1H), 1.93 (s, 3H), 1.92 (s, 3H), 1.23 (s, 3H), 1.12 (d, *J*= 6.6 Hz, 3H), 0.84 (s, 9H), 0.82 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H).

R_f = 0.26 (Hex:EtOAc, 4:1).

Example 34: Compound **13f**



Following the procedure described in example 29, **12g** (342 mg, 0.44 mol) was converted to **13f** (306 mg, 90%, pale yellow oil) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 0:1).

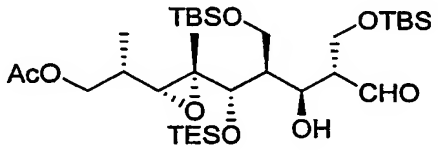
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.64 (d, *J*= 3.3 Hz, 1H), 7.22 (d, *J*= 8.1 Hz, 2H), 6.86 (d, *J*= 8.4 Hz, 2H), 5.64 (dd, *J*= 6.6, 3.9 Hz, 1H), 4.63 (s, 2H), 4.40 (s, 2H), 3.86 (dd, *J*=

9.9, 7.5 Hz, 1H), 3.79 (s, 3H), 3.74 (dd, *J*= 10.2, 4.5 Hz, 1H), 3.65-3.61 (m, 2H), 3.53-3.50 (m, 4H), 3.85-3.34 (m, 1H), 3.37 (s, 3H), 3.21 (d, *J*= 7.2 Hz, 1H), 3.15-3.13 (m, 1H), 2.48 (d, *J*= 9.0 Hz, 1H), 1.98 (s, 3H), 1.80-1.75 (m, 1H), 1.28 (s, 3H), 1.05 (d, *J*= 6.9 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.11 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H).

MS (ESI) m/z: 793 $(M+23)^+$.

R_f = 0.1 (Hex:EtOAc, 4:1).

Example 35: Compound **13g**



Following the procedure described in example 29, **12m** (200 mg, 0.3 mmol) was converted to **13g** (173 mg, 86%, pale yellow oil) after purification of the crude product by flash column chromatography (Hex:EtOAc, 15:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.84 (d, *J*= 2.7 Hz, 1H), 4.67-4.61 (m, 1H), 4.08 (dd, *J*= 11.1, 5.7 Hz, 1H), 3.95-3.84 (m, 3H), 3.81 (d, *J*= 5.1 Hz, 2H), 3.70 (d, *J*= 6.9 Hz, 1H), 3.47 (d, *J*= 5.4 Hz, 1H), 2.64-2.61 (m, 1H), 2.26 (d, *J*= 9.3 Hz, 1H), 2.04 (s, 3H), 1.85-1.80 (m, 1H), 1.30 (s, 3H), 1.11 (d, *J*= 6.6 Hz, 3H), 0.96 (t, *J*= 8.1 Hz, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.68 (q, *J*= 8.1 Hz, 6H), 0.07 (s, 3H), 0.06 (s, 3H), 0.03 (s, 6H).

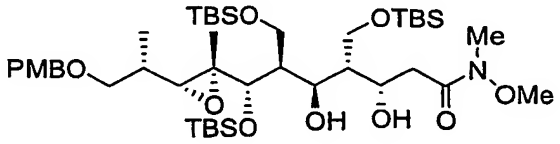
MS (ESI) m/z: 699 $(M+23)^+$, 677 $(M+1)^+$.

R_f = 0.52 (Hex:EtOAc, 4:1).

Example 36: Compounds **14a** and **14b**

To a solution of N-methoxy-N-methylacetamide (0.8 mL g, 7.56 mmol) in THF (2 mL) at -78 °C was added bis-(trimethylsilyl)-lithiumamide (7.56 mL, 1.0 M in THF, 7.56 mmol) and the reaction mixture was stirred for 1 h at -78 °C. Then, a solution of **13a** (1.61 g, 2.13 mmol) in THF (10 mL) was added over the previous solution and the reaction mixture was stirred for an additional 1 h at -78 °C. Then, a saturated aqueous

solution of NH_4Cl (50 mL) was added and the reaction was extracted with EtOAc (3x60 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 4:1 to 2:1) to yield **14a** and **14b** (25:75) as colourless oils (1.67 g, in a combined 91% of yield).

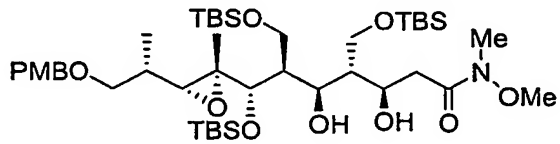


14a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.7 Hz, 2H), 6.85 (d, *J*= 8.7 Hz, 2H), 4.46-4.43 (m, 1H), 4.39 (s, 2H), 4.33 (m, 1H), 4.14 (d, *J*= 7.2 Hz, 1H), 3.92-3.88 (m, 2H), 3.83 (d, *J*= 3.6 Hz, 1H), 3.78 (s, 3H), 3.63 (s, 3H), 3.61-3.57 (m, 3H), 3.41-3.30 (m, 2H), 3.17 (s, 3H), 3.0-2.91 (m, 1H), 2.63-2.62 (m, 1H), 2.58 (d, *J*= 9.0 Hz, 1H), 2.02-1.96 (m, 1H), 1.85-1.78 (m, 1H), 1.75-1.72 (m, 1H), 1.27 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 18H), 0.14 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 159.4, 130.3, 129.3, 114.0, 76.3, 73.0, 72.6, 70.4, 70.1, 64.8, 64.0, 61.9, 61.4, 60.6, 55.4, 47.9, 44.4, 36.9, 34.0, 32.1, 29.9, 26.5, 26.4, 26.1, 26.0, 18.6, 18.3, 18.0, 15.3, 12.8, -4.3, -5.0, -5.1, -5.2, -5.4.

MS (ESI) m/z: 858 $(M+1)^+$.

$[\alpha]^{25}_D$ –10.7 (*c* 0.5, CH_2Cl_2).



14b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, *J*= 8.4 Hz, 2H), 6.83 (d, *J*= 8.4 Hz, 2H), 4.52-4.51 (m, 1H), 4.45 (s, 3H), 4.37 (s, 2H), 4.28-4.23 (m, 1H), 3.91-3.88 (m, 1H), 3.81 (m, 1H), 3.76 (s, 3H), 3.64 (s, 3H), 3.61-3.52 (m, 3H), 3.48-3.43 (dd, *J*= 10.5, 3.3 Hz, 1H), 3.38-3.35 (m, 2H), 3.15 (s, 3H), 2.84-2.79 (m, 1H), 2.57 (d, *J*= 9.0 Hz, 1H), 1.94-1.92 (m, 1H), 1.83-1.81 (m, 1H), 1.72-1.69 (m, 1H), 1.24 (s, 3H), 1.05 (d, *J*= 6.3

Hz, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 159.4, 130.3, 129.2, 113.9, 76.4, 73.0, 72.8, 69.2, 68.5, 64.9, 64.1, 61.4, 60.8, 60.1, 55.4, 47.8, 43.7, 34.1, 26.5, 26.3, 26.2, 26.1, 26.0, 25.9, 18.7, 18.2, 17.9, 15.2, 12.7, -4.6, -4.9, -5.0, -5.2, -5.4, -5.5.

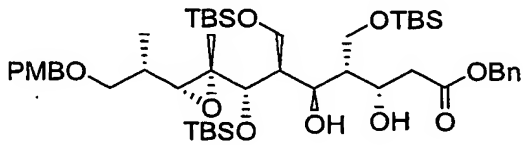
MS (ESI) m/z: 880 $(M+23)^+$, 858 $(M+1)^+$.

$[\alpha]^{25}_D$ +12.8 (*c* 0.50, CH_2Cl_2).

R_f= 0.44 (Hex:EtOAc, 2:1).

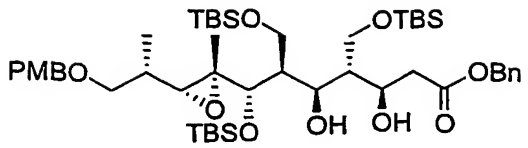
Example 37: Compounds **14c** and **14d**

To a solution of benzyl acetate (38 μL, 0.53 mmol) in dry THF (5 mL) at -78 °C was added lithium bis(trimethylsilyl)amide (264 μL, 1.0 M in THF, 0.264 mmol) and the reaction mixture was stirred for 1 h at –78 °C. Then, a solution of **13a** (150 mg, 0.17 mmol) in THF (5 mL) was added over the previous solution and the reaction mixture was stirred for 5 h at –78 °C. Then, a saturated aqueous solution of NH_4Cl (30 mL) was added and the crude reaction was extracted with EtOAc (3x50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 20:1 to 5:1) to yield **14c** (34 mg, 20%) and **14d** (77mg, 44%) as colourless oils.



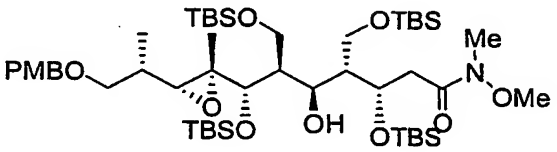
14c: ^1H NMR (300 MHz, $CDCl_3$) δ 7.28-7.39 (m, 5H), 7.19 (d, *J*= 8.7 Hz, 2H), 6.82 (d, *J*= 8.7 Hz, 2H), 5.20 (s, 2H), 5.17 (s, 2H), 4.58-4.64 (m, 1H), 4.38 (s, 2H), 3.78 (s, 3H), 3.58-3.82 (m, 4H), 3.50 (s, 2H), 3.28-3.41 (m, 3H), 2.60 (dd, *J*= 15.0 and 9.6 Hz, 1H), 2.53 (d, *J*= 9.3 Hz, 1H), 2.25 (dd, *J*= 153, 4.7 Hz, 1H), 1.76-1.86 (m, 1H), 1.59-1.62 (m, 1H), 1.26 (s, 3H), 1.05 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.17 (s, 3H), 0.11 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

R_f = 0.33 (Hex:EtOAc, 4:1).



14d: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.55 (m, 5H), 7.20 (d, *J*= 8.7 Hz, 2H), 6.84 (d, *J*= 8.7 Hz, 2H), 5.19 (s, 2H), 4.43-4.48 (m, 1H), 4.40 (s, 2H), 4.32-4.40 (m, 1H), 4.19-4.23 (m, 1H), 3.81 (s, 3H), 3.75-3.98 (m, 3H), 3.42-3.64 (m, 3H), 3.39 (d, *J*= 7.8 Hz, 2H), 2.60 (d, *J*= 9.3 Hz, 1H), 2.61-2.79 (m, 1H), 1.78-1.93 (m, 2H), 1.74-1.77 (m, 1H), 1.25 (s, H), 1.05 (d, *J*= 6.7 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.82-0.92 (m, 6H), 0.49-0.60 (m, 12H), 0.09 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H).
MS (ESI) m/z: 927 $(M+23)^+$.
R_f= 0.30 (Hex:EtOAc, 4:1).

Example 38: Compound **15a**



To a solution of **14a** (1.09 g, 1.26 mmol) in CH_2Cl_2 (20 mL) was added 2,6-lutidine (443 μL, 3.8 mmol) and TBSOTf (437 μL, 1.9 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 40 min. Then, a saturated aqueous solution of NH_4Cl (30 mL) was added, and the reaction was extracted with CH_2Cl_2 (2x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 20:1 to 4:1) to obtain compound **15a** (1.05 g, 85%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 4.87-4.83 (m, 1H), 4.48-4.37 (m, 2H), 4.17-4.14 (m, 2H), 3.86 (dd, *J*= 10.2, 7.0 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.64-3.63 (m, 1H), 3.54 (dd, *J*= 10.2, 3.6 Hz, 1H), 3.53 (dd, *J*= 9.0, 5.1 Hz, 1H), 3.35-3.29 (m, 2H), 3.17 (s, 3H), 3.11-3.05 (m, 1H), 2.56-2.55 (m, 1H), 2.52 (d, *J*= 8.1 Hz, 1H), 2.31-2.28 (m, 1H), 1.84-1.82 (m, 1H), 1.81-1.78 (m, 1H),

1.29 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.15 (s, 6H), 0.1 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.04 (s, 6H), 0.02 (s, 3H).

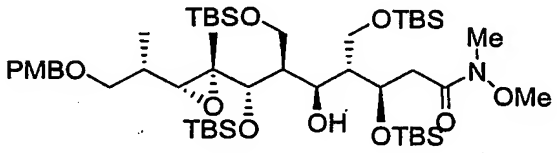
^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 159.4, 130.4, 129.4, 114.0, 76.0, 72.9, 72.4, 69.5, 68.8, 64.6, 64.1, 61.4, 61.0, 59.3, 55.4, 50.1, 43.6, 34.3, 29.9, 26.5, 26.2, 26.1, 26.0, 18.7, 18.3, 17.9, 15.4, 12.7, -4.4, -4.5, -4.6, -4.9, -5.0, -5.2, -5.4, -5.5.

MS (ESI) m/z: 994 $(M+23)^+$, 972 $(M+1)^+$.

$[\alpha]^{25}_D$ –20.0 (*c* 0.5, CH_2Cl_2).

R_f= 0.43 (Hex:EtOAc, 4:1)

Example 39: Compound **15b**



Following the procedure described in example 38, **14b** (2.18 g, 2.52 mmol) was converted to **15b** (2.02 g, 82%, white solid) after purification of the crude product by flash column chromatography (Hex:EtOAc 10:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 4.85-4.82 (m, 1H), 4.44-4.35 (m, 2H), 4.09 (t, *J*= 9.0 Hz, 1H), 3.80 (s, 3H), 3.77-3.73 (m, 1H), 3.65 (s, 3H), 3.63-3.60 (m, 1H), 3.42-3.30 (m, 3H), 3.15 (s, 3H), 2.75-2.72 (m, 1H), 2.61 (d, *J*= 9.3 Hz, 1H), 2.48 (dd, *J*= 15.3, 2.1 Hz, 1H), 1.93-1.88 (m, 1H), 1.84-1.81 (m, 1H), 1.77-1.74 (m, 1H), 1.27 (s, 3H), 1.08 (d, *J*= 6.6 Hz, 3H), 0.90 (s, 3H), 0.88 (s, 18H), 0.85 (s, 9H), 0.13, (s, 3H), 0.09 (s, 3H), 0.08 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H), 0.01 (s, 6H).

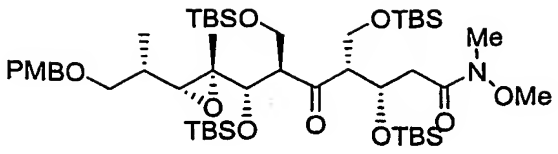
^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 159.4, 130.4, 129.4, 114.0, 76.0, 72.9, 69.5, 68.8, 64.6, 64.1, 61.3, 61.1, 59.3, 55.4, 50.1, 43.5, 34.3, 29.9, 26.5, 26.2, 26.1, 26.0, 18.7, 18.3, 18.2, 17.9, 15.4, 12.7, -4.4, -4.5, -4.6, -4.9, -5.0.

MS (ESI) m/z: 994 $(M+23)^+$, 972 $(M+1)^+$.

$[\alpha]^{25}_D$ +23.1 (*c* 0.50, CH_2Cl_2).

R_f = 0.37 (Hex:EtOAc, 4:1).

Example 40: Compound **16a**



To a solution of **15a** (184 mg, 0.189 mmol) in CH_2Cl_2 (5 mL) was added Dess-Martin periodinane (325 mg, 0.76 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. Saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain **16a** (150 mg, 81 %) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 4.72-4.67 (m, 1H), 4.43 (q, *J*= 11.7 Hz, 2H), 3.80 (s, 3H), 3.78-3.77 (m, 2H), 3.72-3.66 (m, 3H), 3.63 (s, 3H), 3.43-3.38 (m, 1H), 3.32-3.26 (m, 3H), 3.15 (s, 3H), 2.72 (d, *J*= 9.0 Hz, 1H), 2.65 (brd, *J*= 8.7 Hz, 1H), 2.59-2.51 (m, 1H), 1.79-1.72 (m, 1H), 1.32 (s, 3H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.86 (s, 18H), 0.14 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H), 0.00 (s, 6H).

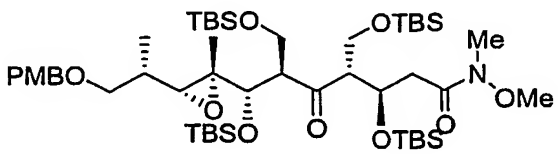
^{13}C NMR (75 MHz, $CDCl_3$) δ 210.7, 172.1, 159.1, 130.3, 129.0, 113.7, 75.9, 72.6, 72.1, 68.1, 63.7, 63.3, 61.4, 61.1, 60.1, 59.9, 57.6, 55.1, 37.2, 33.8, 29.7, 26.1, 26.0, 25.9, 25.8, 18.2, 18.1, 18.0, 15.2, 13.2, -4.3, -4.5, -4.7, -4.9, -5.2, -5.3, -5.4, -5.5.

MS (ESI) m/z: 993 $(M+23)^+$.

$[\alpha]^{25}_D$ –20.3 (*c* 0.50, CH_2Cl_2).

R_f= 0.40 (Hex:EtOAc, 4:1).

Example 41: Compound **16b**



To a solution of **15b** (725 mg, 0.745 mmol) in CH_2Cl_2 (15 mL) was added Dess-Martin periodinane (1.26 g, 2.98 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 2 h. A saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue (720 mg) was used in the next reaction without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (d, *J*= 8.7 Hz, 2H), 6.83 (d, *J*= 8.7 Hz, 2H), 4.68-4.64 (m, 1H), 4.41 (q, *J*= 11.7 Hz, 2H), 3.98-3.85 (m, 3H), 3.76 (s, 3H), 3.67 (dd, *J*= 9.9, 3.0 Hz, 1H), 3.63 (s, 3H), 3.58 (d, *J*= 7.8 Hz, 1H), 3.43 (dd, *J*= 9.3, 6.9 Hz, 1H), 3.30-3.23 (m, 2H), 3.11 (s, 3H), 3.93-2.88 (m, 1H), 2.62-2.57 (m, 2H), 2.55 (d, *J*= 9.3 Hz, 1H), 1.75-1.70 (m, 1H), 1.26 (s, 3H), 1.03 (d, *J*= 6.6 Hz, 3H), 0.87 (s, 9H), 0.84 (s, 9H), 0.83 (s, 9H), 0.82 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H), -0.02 (s, 3H), -0.03 (s, 3H).

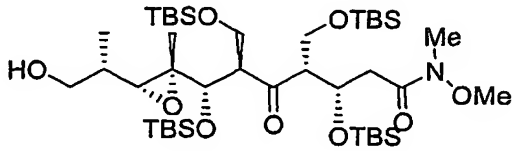
^{13}C NMR (75 MHz, CDCl3) δ 208.4, 171.3, 159.4, 130.6, 129.3, 114.0, 76.0, 72.9, 66.9, 64.1, 63.0, 61.4, 60.7, 60.6, 58.7, 58.5, 55.4, 34.1, 26.4, 26.3, 26.2, 26.1, 26.0, 18.5, 18.4, 18.3, 18.2, 15.5, 14.4, 13.0, -4.3, -4.4, -4.6, -4.7, -4.9, -5.1, -5.2.

MS (ESI) m/z: 992 $(M+23)^+$.

$[\alpha]^{25}_D$ +39.7 (*c* 0.5, CH_2Cl_2).

R_f= 0.45 (Hex:EtOAc, 4:1).

Example 42: Compound **17a**



To a solution of **16a** (289 mg, 0.3 mmol) in a mixture of CH_2Cl_2:H_2O (10:0.5 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (200 mg, 0.89 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 45 min. Saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under

reduced pressure. The residue was solved in MeOH and $NaBH_4$ (35 mg, 0.95 mmol) was added and the reaction was stirred at 23 °C for 30 min. Then, the reaction was concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 6:1) to obtain **17a** (153 mg, 60%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56-4.51 (m, 1H), 3.98-3.74 (m, 4H), 3.64 (s, 3H), 3.61 (bs, 1H), 3.53 (d, *J*=3.9 Hz, 1H), 3.51-3.46 (m, 1H), 3.42-3.37 (m, 1H), 3.23-3.18 (m, 1H), 3.14 (s, 3H), 2.69 (brd, *J*= 6.3 Hz, 1H), 2.65 (brd, *J*= 5.1 Hz, 1H), 2.58 (d, *J*= 9.6 Hz, 1H), 1.72-1.64 (m, 1H), 1.32 (s, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H), 0.05 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.00 (s, 3H).

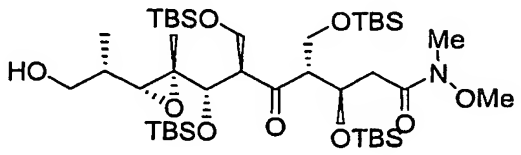
^{13}C NMR (75 MHz, $CDCl_3$) δ 212.7, 171.9, 75.6, 67.6, 65.5, 64.2, 63.2, 61.4, 61.1, 60.9, 60.6, 60.4, 38.1, 35.7, 32.1, 31.9, 29.7, 26.0, 25.9, 18.4, 18.3, 18.1, 18.0, 14.2, 14.2, -4.5, -4.6, -4.7, -5.2, -5.3, -5.4, -5.5.

MS (ESI) m/z: 872 $(M+23)^+$.

$[\alpha]^{25}_D$ –29.5 (*c* 0.5, CH_2Cl_2).

R_f= 0.20 (Hex:EtOAc, 4:1).

Example 43: Compound **17b**



To a solution of crude **16b** (0.745 mmol) in a mixture of CH_2Cl_2:H_2O (10:0.5 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (507 mg, 2.23 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 40 min. Saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was solved in MeOH and $NaBH_4$ (35 mg, 0.95 mmol)

was added in portions during 2 h at 23 °C. Then, the reaction was concentrated under reduced pressure. Saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 6:1) to obtain **17b** (474 mg, 75% for 2 steps) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.58 (dt, *J*= 9.9, 3.0 Hz, 1H), 4.13-3.99 (m, 3H), 3.88 (td, *J*= 9.0, 2.4 Hz, 2H), 3.64 (s, 3H), 3.60 (dd, *J*= 8.7, 4.0 Hz, 1H), 3.54-3.45 (m, 1H), 3.43 (d, *J*= 3.6 Hz, 1H), 3.24 (dt, *J*= 9.9, 3.0 Hz, 1H), 3.15-3.13 (m, 1H), 3.11 (s, 3H), 2.56-2.48 (m, 1H), 2.42 (d, *J*= 9.6 Hz, 1H), 2.30 (dd, *J*= 16.2, 2.4 Hz, 1H), 1.27 (s, 3H), 0.93 (s, 9H), 0.91 (m, 3H), 0.88 (s, 9H), 0.86 (s, 18H), 0.15 (s, 3H), 0.14 (s, 3H), 0.12 (s, 3H), 0.07 (s, 6H), 0.04 (s, 6H), 0.01 (s, 3H).

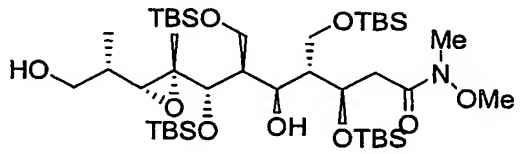
13C NMR (75 MHz, $CDCl_3$) δ 213.0, 171.4, 74.6, 65.7, 65.5, 64.1, 63.6, 63.5, 62.3, 61.1, 60.1, 59.1, 35.9, 34.8, 32.0, 29.6, 26.1, 26.0, 25.8, 25.7, 18.5, 18.3, 17.9, 14.2, 14.0, -4.5, -4.7, -5.0, -5.2, -5.3, -5.5, -5.6.

MS (ESI) m/z: 872 $(M+23)^+$.

$[\alpha]^{25}_D$ –14.4 (*c* 0.5, CH_2Cl_2).

R_f= 0.30 (Hex:EtOAc, 4:1).

Example 44: Compound **17c**

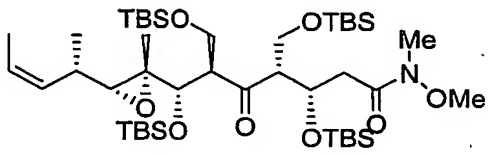


To a solution of **15b** (289 mg, 0.3 mmol) in a mixture of CH_2Cl_2:H_2O (10:0.5 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (200 mg, 0.89 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 30 min. Saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was solved in MeOH and $NaBH_4$ (35 mg, 0.95 mmol) was added and the reaction was stirred at 23 °C for 30 min. Then, the reaction was

concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 7:1) to obtain **17c** (61 mg, 24%) as a white solid.

^1H NMR (300 MHz, $CDCl_3$) δ 4.70-4.66 (m, 1H), 4.05-4.03 (m, 2H), 3.85-3.81 (m, 3H), 3.68 (s, 3H), 3.67-3.65 (m, 1H), 3.50 (br t, *J*= 9.3 Hz, 2H), 3.38 (d, *J*= 7.5 Hz, 1H), 3.18 (bs, 3H), 2.64 (d, *J*= 8.7 Hz, 1H), 2.50 (dd, *J*= 15.0, 1.8 Hz, 1H), 2.09-2.07 (m, 1H), 2.00-1.95 (m, 1H), 1.78-1.77 (m, 1H), 1.27 (s, 3H), 1.09 (d, *J*= 6.9 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), -0.02 (s, 3H).
MS (ESI) m/z: 874 $(M+23)^+$.
R_f= 0.26 (Hex:EtOAc, 4:1).

Example 45: Compound **18a**



To a solution of **17a** (113 mg, 0.13 mmol) in CH_2Cl_2 (2 mL) was added Dess-Martin periodinane (141 mg, 1.33 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 40 min. A saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the corresponding aldehyde (Rf = 0.33 Hex:EtOAc 4:1). Meanwhile, to a suspension of ethyl triphenylphosphonium bromide (395 mg) in toluene (7 mL) was added 1M/THF potassium t-butoxide (0.85 mL) at 0 °C. The resulting orange solution was stirred at 0 °C for 25 min and then cooled to -78 °C. Then, a solution of the fresh crude aldehyde in toluene (5 mL) was added dropwise to the previous suspension at -78 °C and the mixture was allowed to reach 23 °C during 14 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with a saturated

$NaHCO_3$ solution (15 mL). The organic phase was dried over MgSO4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 15:1) to obtain **18a** (80 mg, 70% for 2 steps) as a colourless oil.

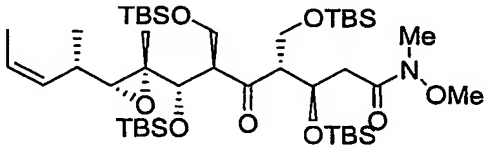
1H NMR (300 MHz, $CDCl_3$) δ 5.52-5.41 (m, 1H), 5.26 (td, *J*= 10.2, 1.5 Hz, 1H), 4.73-4.68 (m, 1H), 3.81 (dd, *J*= 10.5, 4.5 Hz, 1H), 3.75-3.69 (m, 2H), 3.63 (s, 3H), 3.60 (s, 2H), 3.29-3.24 (m, 1H), 3.22-3.16 (m, 1H), 3.14 (s, 3H), 2.71 (d, *J*= 9.3 Hz, 1H), 2.65 (brd, *J*= 7.2 Hz, 1H), 2.52 (dd, *J*= 15.9, 3.3 Hz, 1H), 2.44-2.35 (m, 1H), 1.61 (dd, *J*= 6.9, 1.5 Hz, 3H), 1.29 (s, 3H), 1.10 (d, *J*= 6.3 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 211.2, 172.2, 130.9, 124.2, 76.7, 67.7, 64.9, 62.8, 62.2, 61.1, 60.7, 59.5, 57.3, 37.7, 31.8, 29.7, 26.2, 26.0, 25.9, 25.8, 18.9, 18.3, 18.2, 18.1, 18.1, 13.1, 12.3, -4.3, -4.4, -4.7, -4.9, -5.3, -5.4, -5.5.

MS (ESI) m/z: 882 $(M+23)^+$.

R_f= 0.52 (Hex:EtOAc, 4:1).

Example 46: Compound **18b**



To a solution of **17b** (474 mg, 0.557 mmol) in CH_2Cl_2 (10 mL) was added Dess-Martin periodinane (590 mg, 1.39 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 40 min. A saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the corresponding aldehyde (R_f= 0.38 Hex:EtOAc 4:1). Meanwhile, to a suspension of ethyl triphenylphosphonium bromide (1.64 g) in toluene (15 mL) was added 1M/THF potassium t-butoxide (3.56 mL) at 0 °C. The resulting orange solution was stirred at 0 °C for 25 min and then cooled to -78 °C. Then, a solution of the fresh crude aldehyde in toluene (10 mL) was added dropwise to the

previous suspension at -78 °C and the mixture was allowed to reach 23 °C during 14 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with a saturated $NaHCO_3$ solution (30 mL). The organic phase was dried over MgSO4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 15:1 to 10:1) to obtain **18b** (347 mg, 72% for 2 steps) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51-5.45 (m, 1H), 5.29 (td, *J*= 11.1, 1.5 Hz, 1H), 4.76-4.71 (m, 1H), 3.98 (dd, *J*= 9.6, 3.3 Hz, 1H), 3.90 (dd, *J*= 9.6, 7.2 Hz, 1H), 3.69-3.68 (m, 2H), 3.65 (s, 3H), 3.59 (d, *J*= 8.7 Hz, 1H), 3.36-3.30 (m, 1H), 3.15 (s, 3H), 2.92-2.88 (m, 1H), 2.62 (d, *J*= 9.3 Hz, 1H), 2.58 (d, *J*= 2.1 Hz, 1H), 2.55-2.52 (m, 1H), 2.43-2.35 (m, 1H), 1.61 (dd, *J*= 6.6, 1.5 Hz, 3H), 1.26 (s, 3H), 1.10 (d, *J*=6.6 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.12 (s, 3H), 0.09 (s, 9H), 0.03 (s3H), 0.00 (s, 9H).

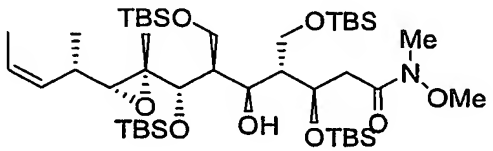
^{13}C NMR (75 MHz, $CDCl_3$) δ 208.63, 172.3, 130.9, 124.2, 76.2, 66.7, 65.0, 62.5, 61.3, 61.1, 60.0, 56.8, 36.7, 31.8, 29.7, 26.2, 25.9, 25.9, 18.9, 18.3, 18.2, 18.1, 18.0, 13.1, 12.0, -4.5, -4.7, -4.8, -4.9, -5.2, -5.3, -5.5.

MS (ESI) m/z: 882 $(M+23)^+$.

$[\alpha]^{25}_D$ +73.9 (*c* 0.5, CH_2Cl_2).

R_f= 0.50 (Hex:EtOAc, 4:1).

Example 47: Compound **18c**

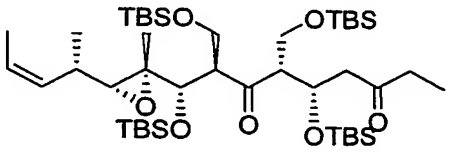


Following the procedure described in example 45, **17c** (60 mg, 0.07 mmol) was converted to **18c** (30 mg, 50%, pale yellow oil) after purification of the crude product by flash column chromatography (Hex:EtOAc 10:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48-5.40 (m, 1H), 5.32-5.25 (m, 1H), 4.85-4.80 (m, 1H), 4.10 (dd, *J*= 11.1, 2.4 Hz, 1H), 4.01 (brt, *J*= 9.0 Hz, 1H), 3.83 (dd, *J*= 10.2, 5.4 Hz,

1H), 3.76 (br d, *J*= 10.8 Hz, 1H), 3.66 (s, 3H), 3.62 (d, *J*= 10.2 Hz, 1H), 3.52 (dd, *J*= 10.2. 6.0 Hz, 1H), 3.37 (d, *J*= 8.4 Hz, 1H), 3.16 (s, 3H), 2.71 (d, *J*= 9.3 Hz, 1H), 2.61-2.58 (m, 1H), 2.50-2.39 (m, 2H), 2.03-2.00 (m, 1H), 1.77 (br d, *J*= 8.4 Hz, 1H), 1.59 (dd, *J*= 6.6, 1.5 Hz, 3H), 1.24 (s, 3H), 1.13 (d, *J*= 6.9 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H), 0.10 (s, 6H), 0.08 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H).
MS (ESI) m/z: 862 $(M+1)^+$.
R_f= 0.48 (Hex:EtOAc, 4:1).

Example 48: Compound **19a**



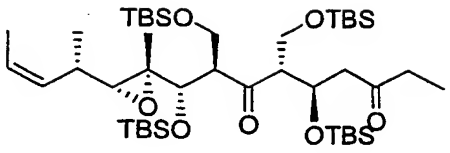
To a solution of **18a** (80 mg, 0.093 mmol) in THF (1.5 mL) was added BrMgEt (0.28 mL, 1.0 M in THF, 0.28 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 30:1) to obtain **19a** (57 mg, 75 %) as a white solid.

^1H NMR (300 MHz, $CDCl_3$) d 5.53-5.43 (m, 1H), 5.26 (td, *J*= 10.2, 1.5 Hz, 1H), 4.71-4.66 (m, 1H), 3.77 (dd, *J*= 10.8, 4.5 Hz, 1H), 3.67 (d, *J*= 5.7 Hz, 2H), 3.60 (t, *J*= 9.3 Hz, 1H), 3.50 (d, *J*= 8.7 Hz, 1H), 3.34-3.27 (m, 1H), 3.20-3.14 (m, 1H), 2.64 (d, *J*= 9 Hz, 1H), 2.58-2.56 (m, 2H), 2.41-2.34 (m, 3H), 1.61 (dd, *J*= 6.6, 1.8 Hz, 3H), 1.29 (s, 3H), 1.10 (d, *J*= 6.3 Hz, 3H), 1.00 (t, *J*= 7.5 Hz, 3H), 0.89 (s, 18H), 0.87 (s, 9H), 0.86 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H), 0.03 (s, 6H), 0.00 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 211.9, 209.2, 130.9, 124.4, 77.3, 67.4, 65.0, 62.7, 62.1, 60.8, 59.8, 57.6, 47.2, 37.1, 31.7, 29.7, 26.3, 26.0, 25.9, 25.8, 18.9, 18.4, 18.3, 18.1, 18.0, 13.1, 12.2, 7.5, -4.2, -4.3, -4.7, -5.0, -5.3, -5.5, -5.6.
MS (ESI) m/z: 851 $(M+23)^+$.

$[\alpha]^{25}_D$ –11.3 (*c* 0.5, CH_2Cl_2).

R_f= 0.74 (Hex:EtOAc, 4:1).

Example 49: Compound **19b**



To a solution of **18b** (347 mg, 0.4 mmol) in THF (4 mL) was added 1M/THF BrMgEt (1.5 mL, 1.5 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. Saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 40:1) to obtain **19b** (280 mg, 84 %) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54-5.44 (m, 1H), 5.30 (td, *J*= 10.2, 1.5 Hz, 1H), 4.71-4.67 (m, 1H), 3.95 (dd, *J*= 9.6, 3.3 Hz, 1H), 3.91-3.85 (m, 1H), 3.69 (d, *J*= 1.5 Hz, 1H), 3.67 (s, 3H), 3.57 (d, *J*= 9.0 Hz, 1H), 3.34-3.27 (m, 1H), 2.89-2.84 (m, 1H), 2.62-2.58 (m, 1H), 2.60 (d, *J*= 9.3 Hz, 1H), 2.44-2.30 (m, 4H), 1.61 (dd, *J*= 6.9, 1.5 Hz, 3H), 1.25 (s, 3H), 1.11 (d, *J*= 6.6 Hz, 3H), 1.02 (t, *J*= 7.5 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.82 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H), 0.01 (s, 3H), 0.00 (s, 9H).

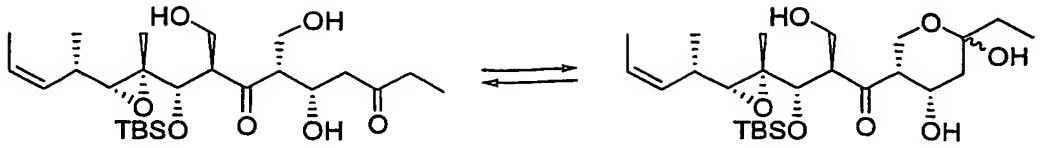
^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 208.7, 130.9, 124.1, 76.0, 65.8, 64.9, 62.3, 61.3, 58.0, 57.2, 46.7, 36.7, 31.8, 26.2, 25.9, 25.8, 18.8, 18.3, 18.2, 18.1, 18.0, 13.1, 12.1, 7.5, -4.5, -4.6, -4.8, -4.9, -5.3, -5.4, -5.5.

MS (ESI) m/z: 851 $(M+23)^+$.

$[\alpha]^{25}_D$ +69.5 (*c* 0.5, CH_2Cl_2).

R_f= 0.76 (Hex:EtOAc, 4:1).

Example 50: Compounds **20a** and **20c**



To a solution of **19a** (160 mg, 0.19 mmol) in THF (6 mL) was added simultaneously TBAF (1.52 mL, 1.0 M in THF, 1.52 mmol) and AcOH (77 μL, 1.35 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 16 h. H_2O (10 mL) was added and the mixture was extracted with EtOAc (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 4:1 to 1:1) to obtain a tautomer equilibrium of **20a** and **20c** (77 mg, 82 %) as a white solid.

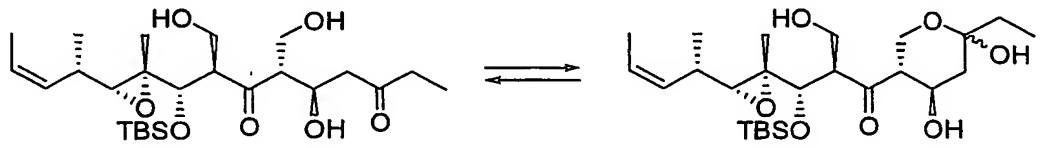
^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.54-5.49 (m, 1H), 5.24 (m, 1H), 4.79 (d, *J*= 2.5 Hz, 1H), 4.30 (dd, *J*= 12.0 Hz, 1H), 3.84 (dd, *J*= 12.5, 4.0 Hz, 1H), 3.67-3.66 (m, 2H), 3.33 (d, *J*= 10.0 Hz, 1H), 3.30-3.26 (m, 1H), 2.77 (ddd, *J*= 11.5, 5.0, 2.5 Hz, 1H), 2.51 (d, *J*= 8.5 Hz, 1H), 2.45-2.39 (m, 1H), 2.02 (dd, *J*= 14.0, 3.5 Hz, 1H), 1.73 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.63 (dd, *J*= 7.0, 1.5 Hz, 3H), 1.61-1.58 (m, 2H), 1.31 (s, 3H), 1.12 (d, *J*= 6.5 Hz, 3H), 0.93 (t, *J*= 7.5 Hz, 3H), 0.86 (s, 9H), 0.11 (s, 3H), -0.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 213.1, 130.5, 124.8, 97.3, 78.6, 65.3, 65.2, 62.2, 61.3, 55.5, 55.2, 54.7, 37.3, 34.5, 31.6, 29.7, 26.0, 18.7, 13.3, 11.4, 7.4, -4.4, -5.2.

MS (ESI) m/z: 509 $(M+23)^+$, 451 $(M+H-2xH_2O)^+$.

R_f= 0.56 (Hex:EtOAc, 1:2).

Example 51: Compounds **20b** and **20d**

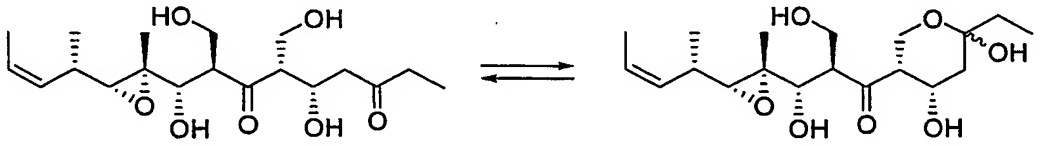


Following the procedure described in example 50, **19b** (35 mg, 0.04 mmol) was converted to a tautomer equilibrium of **20b** and **20d** (12 mg, 60%, pale yellow oil) after

purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.56-5.50 (m, 1H), 5.32-5.26 (m, 1H), 4.38 (ddd, *J*= 15.5, 11.5, 5.0 Hz, 1H), 3.86-3.76 (m, 4H), 3.53 (d, *J*= 9.5 Hz, 1H), 3.24-3.20 (m, 1H), 2.89 (ddd, *J*= 14.5, 11.0, 4.5 Hz, 1H), 2.59 (d, *J*= 9.5 Hz, 1H), 2.46-2.41 (m, 1H), 2.08 (dd, *J*= 12.5, 5.0 Hz, 1H), 1.69-1.66 (m, 2H), 1.64 (dd, *J*= 7.0, 2.0 Hz, 3H), 1.46 (dd, *J*= 13.0, 12.0 Hz, 1H), 1.30 (s, 3H), 1.13 (d, *J*= 7.0 Hz, 3H), 0.97 (t, *J*= 7.5 Hz, 3H), 0.86 (s, 3H), 0.14 (s, 3H), 0.00 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 213.1, 130.6, 124.7, 98.8, 77.0, 66.8, 65.1, 62.2, 60.8, 60.0, 59.0, 40.1, 35.5, 31.5, 29.7, 26.1, 18.8, 18.2, 13.3, 11.5, 7.4, -4.3, -5.0.
MS (ESI) m/z: 509 $(M+23)^+$, 451 $(M+H-2xH_2O)^+$.
$[\alpha]^{25}_D$ +55.0 (*c* 0.5, CH_2Cl_2).
R_f= 0.51 (Hex:EtOAc, 1:2).

Example 52: Compounds **3a** and **4a**



To a solution of **19a** (238 mg, 0.29 mmol) in DMF (5 mL) was added simultaneously TBAF (2.9 mL, 1.0 M in THF, 2.9 mmol) and AcOH (116 μL, 2 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 7 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with EtOAc (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 4:1 to 0:1) to obtain a tautomer equilibrium of **3a** and **4a** (25 mg, 23 %) as a colourless oil.

^{1}H NMR (500 MHz, CD_3OD) (data of the major product) δ 5.56-5.51 (m, 1H), 5.31-5.26 (m, 1H), 4.75 (m, 1H), 4.29 (dd, *J*= 11.5, 11.5 Hz, 1H), 3.72 (dd, *J*= 12.5, 4.0 Hz,

1H), 3.67-3.62 (m, 2H), 3.29-3.27 (m, 1H), 3.16 (d, *J*= 10.0 Hz, 1H), 2.89 (ddd, *J*= 11.5, 4.5, 2.0 Hz, 1H), 2.59 (d, *J*= 9.5 Hz, 1H), 1.93 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.75 (dd, *J*= 14.5, 3.0 Hz, 1H), 1.65 (dd, *J*= 6.5, 2.0 Hz, 3H), 1.56 (q, *J*= 7.5 Hz, 2H), 1.34 (s, 3H), 1.09 (d, *J*= 7.0 Hz, 3H), 0.92 (t, *J*= 7.5 Hz, 3H).

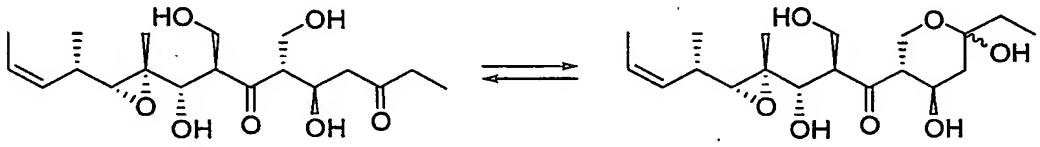
^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.55-5.48 (m, 1H), 5.27-5.20 (m, 1H), 4.74 (brd, *J*= 2.0 Hz, 1H), 4.32 (dd, *J*= 13.0, 13.0 Hz, 1H), 3.89 (dd, *J*= 12.5, 4.0 Hz, 1H), 3.76 (dd, *J*= 10.0, 9.0 Hz, 1H), 3.63 (dd, *J*= 10.5, 3.5 Hz, 1H), 3.33 (d, *J*= 9.5 Hz, 1H), 3.29 (dd, *J*= 9.5, 4.0 Hz, 1H), 2.94 (ddd, *J*= 11.5, 5.0, 2.5 Hz, 1H), 2.68 (d, *J*= 9.0 Hz, 1H), 2.44-2.39 (m, 1H), 2.02 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.73 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.62 (dd, *J*= 7.0, 1.5 Hz, 3H), 1.59-1.56 (m, 2H), 1.33 (s, 3H), 1.11 (d, *J*= 6.0 Hz, 3H), 0.94 (t, *J*= 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 214.2, 130.0, 125.0, 97.3, 77.2, 66.8, 66.7, 65.2, 63.0, 55.6, 54.6, 52.9, 37.1, 34.5, 31.3, 18.6, 13.3, 11.6, 7.4.

MS (ESI) m/z: 767 $(2xM+23)^+$, 395 $(M+23)^+$, 377 $(M+23-H_2O)^+$.

R_f= 0.24 (Hex:EtOAc, 1:2).

Example 53: Compounds **3b** and **4b**



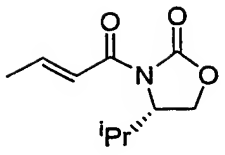
Following the procedure described in example 52, **19b** (200 mg, 0.24 mmol) was converted to a tautomer equilibrium of **3b** and **4b** (20 mg, 21%) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 0:1).

^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) d 5.56-5.48 (m, 1H), 5.28-5.22 (m, 1H), 4.41-4.37 (m, 1H), 3-97-3.73 (m, 5H), 3.34-3.22 (m, 1H), 2.98 (ddd, *J*= 4.5 Hz, 11.5 Hz, 14.5 Hz, 1H), 2.73 (d, *J*= 9 Hz, 1H), 2.46-2.42 (m, 1H), 2.09 (dd, *J*= 5 Hz, 13 Hz, 1H), 1.67 (q, *J*= 7 Hz, 2H), 1.63 (dd, *J*= 1.5 Hz, 7 Hz, 3H), 1.48-1.42 (m, 1H), 1.35 (s, 3H), 1.11 (d *J*= 7 Hz, 3H), 0.96 (t, *J*= 7 Hz, 3H).

MS (ESI) m/z: 395 $(M+23)^+$, 767 $(2M+23)^+$, 377 $(M+23-H_2O)^+$, 337 $(M+1-2H_2O)^+$, 319 $(M+1-3H_2O)^+$. HRMS (TOF) Calcd for $C_{19}H_{32}O_7Na$: 395.2046. Found 395.2019.

R_f= 0.15 (Hex:EtOAc, 1:2).

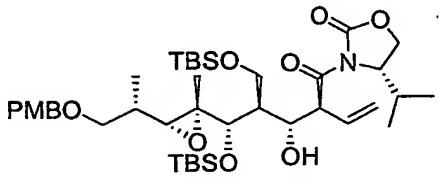
Example 54: Compound **21**



Compound **21** was prepared following the procedure described by D. A. Evans *et al.*, *J. Am. Chem. Soc.* **1984**, *106*, 4261-4263.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (m, 1H), 7.12 (m, 1H), 4.44 (m, 1H), 4.20 (m, 2H), 2.36 (m, 1H), 1.91 (dd, *J*= 6.6, 1.2 Hz, 3H), 0.88 (d, *J*= 6.9 Hz, 3H), 0.83 (d, *J*= 6.9 Hz, 3H).

Example 55: Compound **22**



To a solution of **21** (9.39g, 0.047 mol) in CH_2Cl_2 (75 mL) was added Bu_2BOTf (52.4 mL, 1.0 M in CH_2Cl_2, 52.4 mmol) and Et_3N (9.3 mL, 0.067 mol) at -78 °C. The reaction mixture was stirred 1 h at -78 °C, 15 min at 0 °C and recooled at -78 °C. This solution was added over a solution of **8a** (9 g, 0.016 mol) in CH_2Cl_2 (25 mL) at -50 °C and the mixture was stirred at –50 °C for an additional 10 days. Then, saturated aqueous solution of NH_4Cl (150 mL) was added and the reaction was extracted with CH_2Cl_2 (2x100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 15:1 to 2:1) to afford compound **22** alone with *ca.* 15% of another diastereoisomer (12 g, 80%) as a colourless oil.

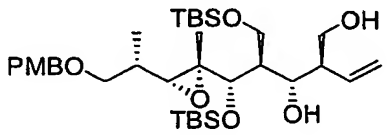
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 6.20 (dt, *J*= 17.4, 10.2 Hz, 1H), 5.25 (dd, *J*= 11.1, 0.6 Hz, 1H), 5.20 (dd, *J*= 19.2, 0.6 Hz, 1H), 4.47-4.33 (m, 3H), 4.28-4.09 (m, 3H), 3.95 (br d, *J*= 3.6 Hz, 1H), 3.80 (s, 3H), 3.65-3.56 (m, 2H), 3.33 (br d, *J*= 7.2 Hz, 2H), 2.90 (d, *J*= 9.3 Hz, 1H), 2.45-2.35 (m, 1H), 2.33-2.23 (q, *J*= 6.9 Hz, 1H), 1.83-1.73 (m, 1H), 1.56-1.46 (m, 1H), 1.28 (s, 3H), 1.03 (d, *J*= 6.9 Hz, 3H), 0.90 (s, 9H), 0.87 (s, *J*= 6.9Hz, 3H), 0.83 (s, *J*= 6.9Hz, 3H), 0.82 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 158.7, 153.0, 132.1, 128.7, 128.3, 118.8, 113.3, 77.0, 74.6, 72.3, 69.0, 64.7, 64.5, 63.0, 62.9, 62.7, 60.0, 58.5, 58.1, 58.0, 54.7, 50.4, 47.1, 32.9, 32.2, 30.9, 28.1, 27.9, 27.3, 25.6, 25.5, 17.8, 17.6, 14.3, 14.3, 14.2, 14.1, -5.1, -5.3, -5.8, -5.9.

MS (ESI) m/z: 786 $(M+23)^+$, 764 $(M+H)^+$.

R_f= 0.32 (Hex:EtOAc, 4:1).

Example 56: Compound **23**



To a solution of the mixture of diastereoisomers (5:1) of **22** (3.9 g, 5.1 mmol) in THF:H_2O (5:1, 75 mL), $LiBH_4$ (13 mL, 2.0 M in THF, 26 mmol) was added at 0 °C. The reaction mixture was stirred 30 min at 0 °C and 2.5 h at 23 °C. Saturated aqueous solution of NH_4Cl (100 mL) was added and the mixture was extracted with EtOAc (3x150 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue **23** (3.4 g) was used in the next step with no further purification.

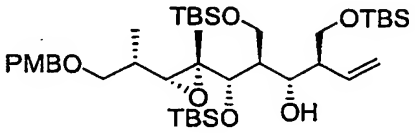
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, *J*= 8.4 Hz, 2H), 6.85 (d, *J*= 9.0 Hz, 2H), 6.17-6.05 (m, 1H), 5.20 (dd, *J*= 10.5, 1.8 Hz, 1H), 5.13 (dd, *J*= 17.7, 1.8 Hz, 1H), 4.40-4.35 (m, 2H), 4.02 (d, *J*= 9.6 Hz, 1H), 3.85-3.73 (m, 2H), 3.80 (s, 3H), 3.48-3.47 (m, 2H), 3.39-3.34 (m, 1H), 3.30-3.24 (m, 1H), 2.66 (d, *J*= 9.3 Hz, 1H), 2.31-2.28 (m, 1H), 1.81-1.74 (m, 2H), 1.28 (s, 3H), 1.05 (d, *J*= 6.6 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H), 0.00 (s, 3H), -0,01 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 135.8, 130.3, 129.2, 118.3, 114.0, 79.1, 73.2, 73.0, 72.3, 67.2, 65.6, 64.4, 60.4, 55.4, 47.7, 46.7, 33.6, 26.2, 18.5, 18.2, 15.0, 12.9, -4.1, -5.0, -5.1, -5.4.

MS (ESI) m/z: 661 $(M+23)^+$, 639 $(M+H)^+$.

R_f= 0.18 (Hex:EtOAc, 4:1).

Example 57: Compound **24**



To a solution of crude **23** (5 mmol) in CH_2Cl_2 (60 mL) was added imidazole (1.02 g, 15 mmol) and TBSCl (1.13 g, 7.5 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 15 min. A saturated aqueous solution of NH_4Cl (70 mL) was added and the reaction was extracted with CH_2Cl_2 (2x100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to obtain pure compound **24** (1.7 g, 43% for two steps) as a colourless oil.

^{1}H NMR (300 MHz, CDCl3) δ 7.19 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 5.96-5.84 (m, 1H), 5.12-5.05 (m, 2H), 4.37 (q, *J*= 11.4 Hz, 2H), 4.0 (d, *J*= 9.3 Hz, 1H), 3.92 (s, 1H), 3.86-3.77 (m, 2H), 3.80 (s, 3H), 3.57-3.46 (m, 3H), 3.37-3.29 (m, 2H), 2.67 (d, *J*= 9.3 Hz, 1H), 2.42-2.36 (m, 1H), 1.83-1.76 (m, 2H), 1.30 (s, 3H), 1.06 (d, *J*= 6.9 Hz, 3H), 0.93 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H), 0.03 (s, 9H), 0.00 (s, 3H).

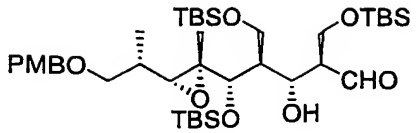
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 136.0, 130.4, 129.2, 118.0, 114.0, 79.2, 73.1, 72.9, 68.2, 65.3, 64.7, 64.6, 60.7, 55.4, 49.1, 47.1, 33.6, 26.3, 26.2, 26.1, 18.5, 15.1, 12.9, -4.1, -4.9, -5.1, -5.2, -5.3.

MS (ESI) m/z: 775 $(M+23)^+$, 753 $(M+H)^+$.

$[\alpha]^{25}_D$ –8.0 (*c* 0.50, CH_2Cl_2).

R_f= 0.65 (Hex:EtOAc, 4:1).

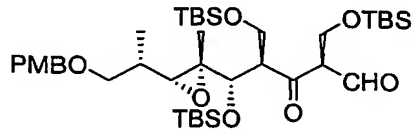
Example 58: Compound **25a**



Over a solution of **24** (1.58 g, 2.09 mmol) in CH_2Cl_2 (40 mL) was bubbled a current of O_3 during 2 min at -78 °C. Then, Ph_3P (1.65 g, 6.27 mmol) was added and the mixture was allowed to warm to room temperature, and the stirring was continued for 1.5 h. The mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to afford compound **25a** (1.34 g, 85%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (d, *J*= 3.0 Hz, 1H), 7.21 (d, *J*= 8.7 Hz, 2H), 6.89 (d, *J*= 8.7 Hz, 2H), 4.39 (s, 2H), 4.18 (dd, *J*= 9.9, 7.8 Hz, 1H), 4.08 (m, 1H), 4.04-4.03 (m, 1H), 3.90 (dd, *J*= 9.9, 6.0 Hz, 1H), 3.81 (s, 3H), 3.73-3.68 (m, 2H), 3.55-3.50 (dd, *J*= 10.5, 3.3 Hz, 1H), 3.40-3.27 (m, 2H), 2.67 (d, *J*= 9.3 Hz, 1H), 2.62 (m, 1H), 1.98-1.92 (m, 1H), 1.83-1.74 (m, 1H), 1.27 (s, 3H), 1.05 (d, *J*= 6.9 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.17 (s, 3H), 0.11 (s, 3H),0.05 (s, 6H), 0.02 (s, 3H), 0.00 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 159.4, 130.3, 129.4 114.1, 79.2, 73.2, 72.9, 70.4, 65.5, 64.0, 61.7, 60.9, 55.8, 55.4, 47.4, 33.6, 26.2, 26.0, 18.4, 18.2, 15.0, 12.9, -4.1, -5.0, -5.2, -5.3, -5.3, -5.4.
MS (ESI) m/z: 777 $(M+23)^+$.
$[\alpha]^{25}_D$ –7.9 (*c* 0.52, CH_2Cl_2).
R_f= 0.67 (Hex:EtOAc, 4:1).

Example 59: Compound **25b**

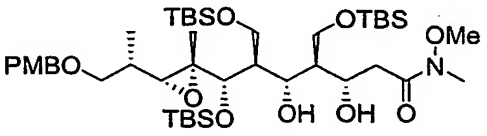


To a solution of **25a** (1.34 mg, 1.78 mmol) in CH_2Cl_2 (50 mL) was added Dess-Martin periodinane (1.5 mg, 3.56 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The

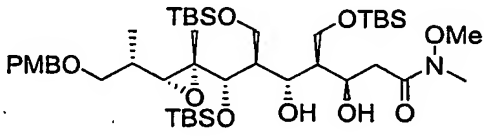
reaction mixture was stirred at 23 °C for 50 min. A saturated aqueous solution of $NaHCO_3$ (60 mL) was added and the mixture was extracted with CH_2Cl_2 (3x70 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give aldehyde **25b** which was used in the next step with no further purification.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.59 (d, J = 2.7 Hz, 1H), 7.23 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 4.36-4.48 (m, 2H), 4.22-4.29 (m, 1H), 3.98-4.07 (m, 1H), 3.81-3.88 (m, 1H), 3.80 (s, 3H), 3.64-3.78 (m, 2H), 3.32-3.45 (m, 4H), 2.47 (d, J = 9.3 Hz, 1H), 1.68-1.81 (m, 1H), 1.24 (s, 3H), 1.03 (d, J = 6.7 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), -0.01 (s, 3H), -0.02 (s, 3H). R_f = 0.69 (Hex:EtOAc, 4:1).

Example 60: Compounds **26a** and **26b**



26a



26b

To a solution of N-methoxy-N-methylacetamide (70 µL g, 0.65 mmol) in THF (2 mL) at -78 °C was added bis-(trimethylsilyl)-lithiumamid (0.65 mL, 1.0 M in THF, 0.65 mmol) and the reaction mixture was stirred for 1 h at that temperature. Then, a solution of **25a** (165 mg, 0.22 mmol) in THF (4 mL) was added over the previous solution and the reaction mixture was stirred for an additional 1 h at -78 °C. Then, a saturated aqueous solution of NH_4Cl (30 mL) was added and the reaction was extracted with EtOAc (3x50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 4:1 to 1:1) to yield **26a** and **26b** (1:2) as colourless oils (139 mg, in a combined 74%of yield).

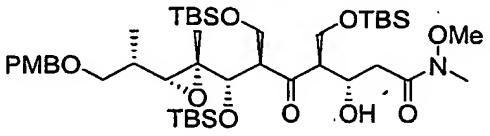
^{1}H NMR (300 MHz, $CDCl_3$) mix of diastereoisomers δ 7.19-7.25 (m, 2H), 6.82-6.89 (m, 2H), 4.58-4.63 (m, 1H), 4.36-4.55 (m, 2H), 4.01-4.08 (m, 1H), 5.75-5.98 (m, 3H),

3.80 (s, 1.98H), 3.79 (s, 1.02H), 3.65 (s, 1.98H), 3.64 (s, 1-02H), 3.44-3.65 (m, 2H), 3.25-3.32 (m, 2H), 3.17 (s, 1.02H), 3.16 (s, 1.98H), 2.80-2.88 (m, 1H), 2.69 (d, J = 9.3 Hz, 0.66H), 2.68 (d, J = 9.0 Hz, 0.34H), 2.65-2.74 (m, 1H), 2.00-2.09 (m, 1H), 1.74-1.88 (m, 2H), 1.69 (br s, 1H), 1-34 (s, 1.02H), 1.25 (s, 1.98H), 1.07 (m, 3H), 0.92 (s, 5.94H), 0.90 (s, 3.06H), 0.89 (s, 3.06H), 0.88 (s, 5.94H), 0.85 (s, 3.06H), 0.83 (s, 5.94H), -0.02-0.18 (m, 18H).

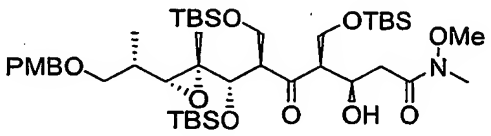
MS (ESI) m/z: 880 $(M+23)^+$, 858 $(M+1)^+$.

R_f = 0.09 (Hex:EtOAc, 4:1).

Example 61: Compounds **26c** and **26d**



26c



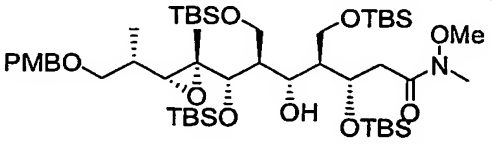
26d

To a solution of N-methoxy-N-methylacetamide (568 µL g, 5.34 mmol) in THF (15 mL) at -78 °C was added bis-(trimethylsilyl)-lithiumamid (1.0 M in THF) (5.34 mL, 5.34 mmol) and the reaction mixture was stirred for 1 h at that temperature. Then, a solution of crude **25b** (1.78 mmol) in THF (25 mL) was added over the previous solution and the reaction mixture was stirred for an additional 3 h at -78 °C. Then, a saturated aqueous solution of NH_4Cl (50 mL) was added and the reaction was extracted with EtOAc (3x60 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 4:1 to 2:1) to yield **26c** and **26d** (1:1.9) as colourless oils (910 mg, in a combined 60% of yield for two steps).

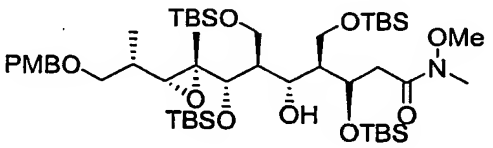
^{1}H NMR (300 MHz, $CDCl_3$) mix of diastereoisomers δ 7.25 (d, J= 8.7 Hz, 4H), 6.88 (d, J= 8.4 Hz, 4H), 4.64-4.60 (m, 1H), 4.48-4.36 (m, 6H), 4.10-3.82 (m, 6H), 3.80 (s, 6H), 3.76-3.71 (m, 2H), 3.66 (s, 6H), 3.61 (d, J= 3.3 Hz, 1H), 3.53-3.48 (m, 2H), 3.44-3.29 (m, 6H), 3.18 (s, 6H), 3.01-2.80 (m, 3H), 2.61 (m, 1H), 2.57 (d, J= 9.0 Hz, 1H), 2.53 (d, J= 9.0 Hz, 1H), 1.81-1.67 (m, 2H), 1.32 (s, 3H), 1.31 (s, 3H), 1.05 (d, J= 6.9 Hz, 6H),

0.89 (s, 18 H), 0.87 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.1 (s, 6H), 0.07 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H), 0.01 (s, 6H), 0.00 (s, 3H), -0.01 (s, 3H), -0.01 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 172.4, 159.0, 130.1, 128.9, 113.6, 77.0, 72.6, 72.0, 71.9, 67.4, 66.1, 64.1, 64.0, 63.1, 63.0, 61.0, 60.8, 60.5, 60.1, 59.8, 58.9, 56.7, 55.1, 36.3, 33.5, 26.0, 25.7, 18.2, 18.0, 15.0, 12.5, -4.6, -4.7, -5.0, -5.1, -5.5, -5.6.
MS (ESI) m/z: 878 $(M+23)^+$.
R_f= 0.44 (Hex:EtOAc, 2:1). Also R_f = 0.16 (Hex:EtOAc, 4:1).

Example 62: Compounds **27a** and **27b**



27a



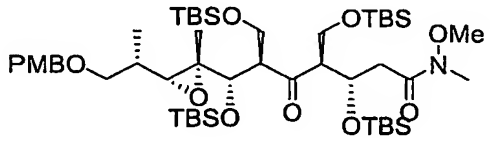
27b

To a solution of a mixture of **26a** and **26b** (139 mg, 0.16 mmol) in CH_2Cl_2 (8 mL) was added 2,6-lutidine (57 μL, 0.49 mmol) and TBSOTf (56 μL, 0.24 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then, a saturated aqueous solution of NH_4Cl (30 mL) was added, and the reaction was extracted with CH_2Cl_2 (2x25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc 10:1) to obtain **27a** (white solid) and **27b** (colourless oil) (1:2) (113 mg in a combined 72% of yield).

27a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 4.66 (brd, *J*= 9.9 Hz, 1H), 4.50 (dd, *J*= 11.7 Hz, 2H), 4.10 (brd, *J*= 9.6 Hz, 1H), 3.92 (d, *J*= 6.6 Hz, 2H), 3.80 (s, 3H), 3.66 (s, 3H), 3.64-3.59 (m, 2H), 3.42-3.85 (m, 1H), 3.35-3.32 (m, 1H), 3.15 (s, 3H), 3.01-2.96 (m, 1H), 2.74 (d, *J*= 9.3 Hz, 1H), 2.70-2.67 (m, 1H), 2.08-2.03 (m, 1H), 1.92 (bs, 1H), 1.79-1.70 (m, 1H), 1.37 (s, 3H), 1.07 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H), 0.08 (s, 3H), 0.03 (s, 6H), 0.02 (s, 6H), 0.00 (s, 3H).
MS (ESI) m/z: 994 $(M+23)^+$.
R_f = 0.34 (Hex:EtOAc, 4:1).

27b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 4.82-4.80 (m, 1H), 4.43 (q, *J*= 11.4 Hz, 2H), 3.96-3.92 (m, 1H), 3.80 (s, 3H), 3.76-3.75 (m, 1H), 3.66 (s, 3H), 3.69-3.58 (m, 3H), 3.46 (dd, *J*= 9.0, 6.3 Hz, 1H), 3.31 (dd, *J*= 9.0, 7.2 Hz, 1H), 3.15 (s, 3H), 3.00-2.93 (m, 1H), 2.69 (d, *J*= 8.7 Hz, 1H), 2.69-2.62 (m, 1H), 2.02-1.94 (m, 2H), 1.80-1.73 (m, 1H), 1.65 (s, 1H), 1.33 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.02 (s, 3H).
MS (ESI) m/z: 994 $(M+23)^+$.
R_f = 0.46 (Hex:EtOAc, 4:1).

Example 63: Compound **27c**

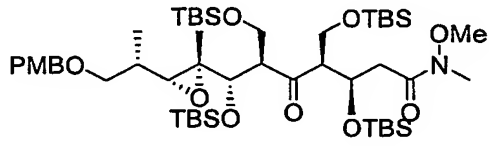


To a solution of **27a** (36 mg, 0.04 mmol) in CH_2Cl_2 (4 mL) was added Dess-Martin periodinane (63 mg, 0.15 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 1.5 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain **27c** (26 mg, 72%) as a pale yellow oil. This

compound is also obtained by protection of **26c** with TBSOTf and lutidine with a quantitative yield under standard condition.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, *J*= 8.7 Hz, 2H), 6.86 (d, *J*= 8.7 Hz, 2H), 4.80-4.78 (m, 1H), 4.41 (q, *J*= 11.4 Hz, 2H), 4.15 (d, *J*= 4.5 Hz, 2H), 3.80 (s, 3H), 3.75-3.67 (m, 2H), 3.64 (s, 3H), 3.61-3.50 (m, 3H), 3.39 (dd, *J*= 9.3, 7.2 Hz, 1H), 3.29 (dd, *J*= 9.3, 6.6 Hz, 1H), 3.15 (bs, 3H), 2.99-2.96 (m, 1H), 2.67 (d, *J*= 9.3 Hz, 1H), 2.54 (br d, *J*= 5.1 Hz, 1H), 1.33 (s, 3H), 1.06 (d, *J*= 6.3 Hz, 3H), 0.90 (s, 9H), 0.85 (s, 18H), 0.84 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H), 0.01 (s, 6H), -0.01 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 172.5, 159.1, 130.2, 128.9, 113.7, 76.1, 72.6, 72.1, 67.0, 64.0, 63.8, 61.5, 61.0, 60.8, 58.1, 55.1, 54.2, 36.7, 33.6, 29.6, 26.0, 25.9, 25.8, 25.7, 18.2, 18.1, 18.0, 17.9, 15.1, 13.4, -4.8, -4.9, -4.9, -5.4, -5.5, -5.5, -5.6.
MS (ESI) m/z: 992 $(M+23)^+$, 970 $(M+1)^+$.
$[\alpha]^{25}_D$ –45.1 (*c* 0.50, CH_3Cl).
R_f = 0.38 (Hex:EtOAc, 4:1).

Example 64: Compound **27d**



To a solution of **27b** (77 mg, 0.08 mmol) in CH_2Cl_2 (3 mL) was added Dess-Martin periodinane (63 mg, 0.15 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 1.5 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain **27d** (51 mg, 66 %) as a pale yellow oil. This compound is also obtained by protection of **26d** with TBSOTf and lutidine with a quantitative yield under standard condition.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.7 Hz, 2H), 6.87 (d, *J*= 8.7 Hz, 2H), 4.47 (d, *J*= 12.0 Hz, 1H), 4.36 (d, *J*= 12.0 Hz, 1H), 3.99-3.83 (m, 3H), 3.80 (s, 3H), 3.69-3.58 (m, 2H), 3.68 (s, 3H), 3.42-3.36 (m, 2H), 3.26 (dd, *J*= 9.3, 6.3 Hz, 1H), 3.17 (bs, 3H), 3.07 (dt, *J*= 9.3, 3.3 Hz, 1H), 2.90-2.87 (m, 1H), 2.59 (d, *J*= 9.0 Hz, 1H), 2.17 (br d, *J*= 14.1 Hz, 1H), 1.31 (s, 3H), 1.05 (d, *J*= 6.6 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.18 (s, 3H), 0.12 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), -0.01 (s, 6H), -0.02 (s, 3H).

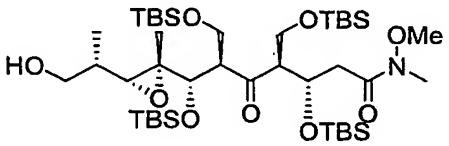
^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 172.1, 159.2, 130.2, 129.0, 113.8, 76.3, 72.5, 71.8, 68.2, 64.2, 63.0, 61.3, 60.9, 60.0, 59.3, 57.7, 55.1, 36.4, 34.0, 29.6, 26.4, 25.9, 25.8, 25.7, 18.7, 18.1, 17.9, 15.3, 12.4, -4.3, -4.4, -5.1, -5.2, -5.5, -5.6, -5.7.

MS (ESI) m/z: 992 $(M+23)^+$.

$[\alpha]^{25}_D$ +47.6 (*c* 0.5, CH_3Cl).

R_f = 0.45 (Hex:EtOAc, 4:1).

Example 65: Compound **28a**



To a solution of **27c** (390 mg, 0.4 mmol) in a mixture of CH_2Cl_2:H_2O (4:0.2 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (274 mg, 1.2 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 18 min. Saturated aqueous solution of $NaHCO_3$ (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was solved in MeOH and $NaBH_4$ (74 mg, 2 mmol) was added and the reaction was stirred at 23 °C for 30 min. Then, the reaction was concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 4:1) to obtain **28a** (220 mg, 65%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77-4.72 (m, 1H), 4.10-3.99 (m, 2H), 3.86-3.84 (m, 2H), 3.65 (s, 3H), 3.62-3.59 (m, 1H), 3.56-3.48 (m, 3H), 3.15 (s, 3H), 2.99-2.95 (m, 1H), 2.76-2.75 (m, 1H), 2.58-2.55 (m, 1H), 2.52 (br d, *J*= 3.3 Hz, 1H), 2.46 (d, *J*= 9.3 Hz, 1H), 1.67 (bs, 1H), 1.37 (s, 3H), 1.01 (d, *J*= 6.9 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H).

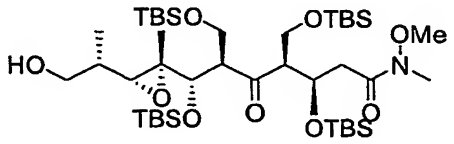
^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8, 172.1, 76.9, 67.1, 65.1, 64.8, 63.4, 61.5, 61.2, 61.1, 58.5, 57.3, 36.6, 35.8, 32.0, 29.6, 26.0, 25.9, 25.8, 25.7, 18.2, 18.1, 17.9, 14.3, 13.7, -4.6, -4.8, -5.2, -5.4, -5.5, -5.6.

MS (ESI) m/z: 872 $(M+23)^+$.

$[\alpha]^{25}_D$ –32.9 (*c* 0.50, CH_3Cl).

R_f = 0.31 (Hex:EtOAc, 4:1).

Example 66: Compound **28b**



To a solution of **27d** (718 mg, 0.74 mmol) in a mixture of CH_2Cl_2:H_2O (10:0.5 mL) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (504 mg, 2.22 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 17 min. Saturated aqueous solution of $NaHCO_3$ (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was solved in MeOH and $NaBH_4$ (110 mg, 3 mmol) was added and the reaction was stirred at 23 °C for 20 min. Then, the reaction was concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 4:1) to obtain **28b** (374 mg, 60%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75-4.72 (m, 1H), 4.02-3.92 (m, 2H), 3.88 (dd, *J*= 10.5, 3.9 Hz, 1H), 3.71-3.65 (m, 1H), 3.67 (s, 3H), 3.61-3.54 (m, 2H), 3.49 (d, *J*= 6.3 Hz, 1H), 3.45-3.39 (m, 1H), 3.16 (bs, 3H), 3.13-3.08 (m, 1H), 2.84 (br dd, *J*= 15.9, 8.7 Hz, 1H), 2.48 (d, *J*= 9.0 Hz, 1H), 2.46-2.44 (m, 1H), 1.72-1.67 (m, 1H), 1.31 (s, 3H), 1.09 (d, *J*= 6.6 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H).

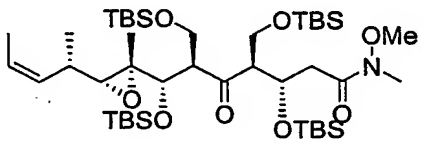
^{13}C NMR (75 MHz, $CDCl_3$) δ 212.6, 172.0, 76.4, 67.6, 65.2, 65.0, 62.9, 61.2, 61.1, 60.8, 59.9, 59.5, 37.1, 36.2, 32.0, 29.6, 26.0, 25.9, 25.8, 25.6, 18.3, 18.1, 18.0, 18.0, 14.4, 13.5, -3.6, -4.4, -4.8, -4.9, -5.0, -5.5, -5.6, -5.7.

MS (ESI) m/z: 872 $(M+23)^+$.

$[\alpha]^{25}_D$ +21.6 (*c* 0.52, CH_3Cl).

R_f = 0.31 (Hex:EtOAc, 4:1).

Example 67: Compound **29a**



To a solution of **28a** (162 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) was added Dess-Martin periodinane (202 mg, 0.47 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 40 min. A saturated aqueous solution of $NaHCO_3$ (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the corresponding aldehyde (R_f= 0.32, Hex:EtOAc, 4:1). Meanwhile, to a suspension of ethyl triphenylphosphonium bromide (565 mg, 1.94 mmol) in toluene (7 mL) was added potassium t-butoxide (1.24 mL, 1.0 M in THF, 1.24 mmol) at 0 °C. The resulting orange solution was stirred at 0 °C for 25 min and then cooled to -78 °C. Then, a solution of the fresh crude aldehyde in toluene (5 mL) was added dropwise to the previous suspension at -78 °C and the mixture was allowed to reach 23 °C during 14 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with a saturated $NaHCO_3$ solution (30 mL). The organic phase was dried over

MgSO4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 20:1) to obtain **29a** (105 mg, 64% for 2 steps) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52-5.46 (m, 1H), 5.26-5.19 (m, 1H), 4.88-4.87 (m, 1H), 4.20-4.09 (m, 2H), 3.70-3.65 (m, 1H), 3.64 (s, 3H), 3.60-3.57 (m, 3H), 3.42 (d, *J*= 8.4 Hz, 1H), 3.15 (bs, 3H), 2.79-2.75 (m, 1H), 2.58 (d, *J*= 9.6 Hz, 1H), 2.43-2.39 (m, 2H), 1.62 (dd, *J*= 6.6, 1.5 Hz, 3H), 1.29 (s, 3H), 1.10 (d, *J*= 6.6 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), -0.01 (s, 3H), -0.02 (s, 3H).

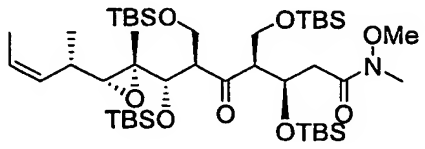
^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 171.9, 130.5, 124.0, 66.6, 64.8, 62.6, 61.9, 61.6, 60.6, 57.0, 53.7, 36.2, 31.1, 29.2, 25.7, 25.5, 25.4, 25.3, 18.4, 17.8, 17.7, 17.6, 12.7, 11.8, -5.1, -5.2, -5.3, -5.4, -5.8, -5.9, -6.0.

MS (ESI) m/z: 882 $(M+23)^+$.

$[\alpha]^{25}_D$ –26.1 (*c* 0.50, CH_2Cl_2).

R_f= 0.44 (Hex:EtOAc, 4:1).

Example 68: Compound **29b**



To a solution of **28b** (318 mg, 0.37 mmol) in CH_2Cl_2 (8 mL) was added Dess-Martin periodinane (397 mg, 0.93 mmol) and catalytic amount of $NaHCO_3$ at 23 °C. The reaction mixture was stirred at 23 °C for 40 min. A saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the corresponding aldehyde (R_f= 0.42, Hex:EtOAc, 4:1). Meanwhile, to a suspension of ethyl triphenylphosphonium bromide (1.1 g, 3.77 mmol) in toluene (12 mL) was added potassium t-butoxide (2.43 mL, 1M in THF, 2.34 mmol) at 0 °C. The resulting orange solution was stirred at 0 °C for 25 min and then cooled to -78 °C. Then, a solution of the fresh crude aldehyde in toluene (6 mL) was added

dropwise to the previous suspension at -78 °C and the mixture was allowed to reach 23 °C during 15 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with a saturated $NaHCO_3$ solution (30 mL). The organic phase was dried over MgSO4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc 20:1) to obtain **29b** (195 mg, 60% for 2 steps) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.50-5.42 (m, 1H), 5.29-5.25 (m, 1H), 4.81-4.78 (m, 1H), 3.93 (dd, *J*= 11.4, 3.6 Hz, 1H), 3.81 (m, 2H), 3.67 (s, 3H), 3.64-3.56 (m, 2H), 3.43-3.39 (m, 1H), 3.17 (bs, 3H), 3.03-3.00 (m, 1H), 2.96-2.88 (m, 1H), 2.65 (d, *J*= 9.0 Hz, 1H), 2.46-2.35 (m, 1H), 2.10 (br d, *J*= 14.7 Hz, 1H), 1.61 (dd, *J*= 6.9, 1.8 Hz, 1H), 1.28 (s, 3H), 1.11 (d, *J*= 6.9 Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.84 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.06 (s, 3H), 0.01 (s, 3H), -0.02 (s, 3H), -0.03 (s, 3H).

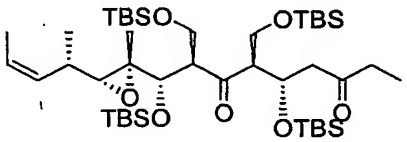
^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 172.0, 131.0, 124.2, 76.3, 68:1, 65.0, 62.6, 61.4, 61.3, 59.6, 59.4, 57.2, 36.3, 31.8, 29.7, 26.4, 25.9, 25.8, 25.7, 18.9, 18.7, 18.1, 18.0, 17.9, 13.2, 11.9, -4.3, -4.4, -5.1, -5.2, -5.4, -5.5, -5.6.

MS (ESI) m/z: 882 $(M+23)^+$.

$[\alpha]^{25}_D$ +70.2 (*c* 0.50, CH_2Cl_2).

R_f= 0.77 (Hex:EtOAc, 4:1).

Example 69: Compound **30a**

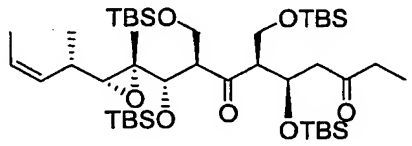


To a solution of **29a** (80 mg, 0.093 mmol) in THF (1.5 mL) was added BrMgEt (0.28 mL, 1M in THF, 0.28 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 3 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified

by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to obtain **30a** (54 mg, 71 %) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54-5.44 (m, 1H), 5.26-5.18 (m, 1H), 4.83 (ddd, *J*= 9.6, 4.2, 21. Hz, 1H), 4.13 (dd, *J*= 9.6, 7.2 Hz, 1H), 4.05 (dd, *J*= 9.6, 3.9 Hz, 1H), 3.67 (dd, *J*= 8.7, 6.6 Hz, 1H), 3.59-3.57 (m, 2H), 3.38 (d, *J*= 9.0 Hz, 1H), 2.75-70 (m, 1H), 2.55 (d, *J*= 9.3 Hz, 1H), 2.46-2.43 (m, 5H), 1.62 (dd, *J*= 6.6, 1.8 Hz, 3H), 1.28 (s, 3H), 1.10 (d, *J*= 6.3 Hz, 3H), 1.01 (t, *J*= 7.2 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.82 (s, 9H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), -0.01 (s, 3H), -0.03 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 212.5, 209.2, 131.1, 124.7, 78.2, 66.6, 65.5, 63.2, 62.6, 62.4, 57.5, 54.3, 53.6, 47.3, 36.7, 31.8, 29.9, 26.3, 26.1, 26.0, 19.0, 18.5, 18.3, 18.2, 13.4, 12.4, 7.8, -4.3, -4.4, -4.7, -4.8, -5.1, -5.2, -5.3.
MS (ESI) m/z: 851 $(M+23)^+$.
$[\alpha]^{25}_D$ –25.4 (*c* 0.50, CH_2Cl_2).
R_f= 0.86 (Hex:EtOAc, 4:1).

Example 70: Compound **30b**



To a solution of **29b** (110 mg, 0.13 mmol) in THF (1.5 mL) was added BrMgEt (0.38 mL, 1M in THF, 0.38 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 4 h. Saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 20:1) to obtain **30b** (70 mg, 65 %) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52-5.41 (m, 1H), 5.28-5.20 (m, 1H), 4.76-4.72 (m, 1H), 3.85-3.73 (m, 3H), 3.70 (d, *J*= 10.2 Hz, 1H), 3.48-3.41 (m, 2H), 3.05-3.00 (dt, *J*=

10.2, 3.3 Hz, 1H), 2.80 (dd, *J*= 15.6, 10.5 Hz, 1H), 2.64 (d, *J*= 9.3 Hz, 1H), 2.45-2.40 (m, 3H), 2.38-2.12 (m, 1H), 1.61 (dd, *J*= 6.9, 1.8 Hz, 3H), 1.29 (s, 3H), 1.11 (d, *J*= 6.3 Hz, 3H), 1.01 (t, *J*= 7.2 Hz, 3H), 0.89 (s, 18H), 0.84 (s, 18H), 0.19 (s, 3H), 0.14 (s, 3H), 0.05 (s, 3H), 0.03 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H), -0.04 (s, 3H).

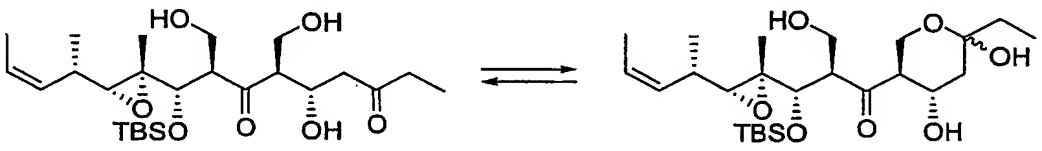
^{13}C NMR (75 MHz, $CDCl_3$) δ 209.5, 209.3, 131.0, 124.3, 76.0, 67.6, 64.9, 62.4, 61.3, 59.8, 58.9, 57.3, 45.5, 38.1, 31.9, 29.7, 26.3, 25.9, 25.8, 25.7, 19.0, 18.7, 18.1, 18.0, 17.8, 13.3, 11.9, 7.4, -4.1, -4.2, -5.1, -5.2, -5.4, -5.5, -5.6, -5.7.

MS (ESI) m/z: 851 $(M+23)^+$.

$[\alpha]^{25}_D$ +80.9 (*c* 0.50, CH_2Cl_2).

R_f= 0.71 (Hex:EtOAc, 4:1).

Example 71: Compounds **31a** and **31c**



Following the procedure described in example 50, **30a** (48 mg, 0.058 mmol) was converted to a tautomer equilibrium of **31a** and **31c** (20 mg, 70%, colourless oil) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 1:1).

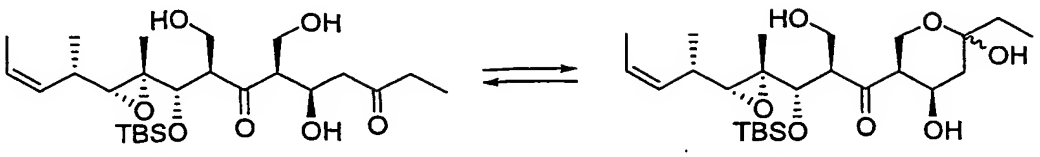
^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) d 5.55-5.49 (m, 1H), 5.29-5.24 (m, 1H), 4.28 (ddd, *J*= 15.5, 11.0, 4.5 Hz, 1H), 3.97 (dd, *J*= 11.5, 11.5 Hz, 2H), 3.76 (dd, *J*= 11.5, 3.5 Hz, 1H), 3.67-3.65 (m, 1H), 3.62 (d, *J*= 10.0 Hz, 1H), 3.35-3.31 (m, 1H), 2.86-2.80 (m, 1H), 2.60 (d, *J*= 9.0 Hz, 1H), 2.44-2.37 (m, 1H), 2.09 (dd, *J*= 12.5, 4.5 Hz, 1H), 1.70-1.65 (m, 2H), 1.62 (dd, *J*= 7.0, 2.0 Hz, 3H), 1.45 (br t, *J*= 11.5 Hz, 1H), 1.30 (s, 3H), 1.11 (d, *J*= 7.0 Hz, 3H), 0.96 (t, *J*= 7.5 Hz, 3H), 0.89 (s, 9H), 0.16 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 214.7, 130.5, 124.8, 98.7, 78.2, 66.9, 65.0, 61.8, 60.5, 59.6, 59.2, 57.7, 39.9, 35.6, 31.4, 26.1, 18.7, 18.4, 13.3, 11.6, 7.4, -4.4, -4.7.

MS (ESI) m/z: 509 $(M+23)^+$, 451 $(M+1-2xH_2O)^+$.

R_f= 0.4 (Hex:EtOAc, 1:2).

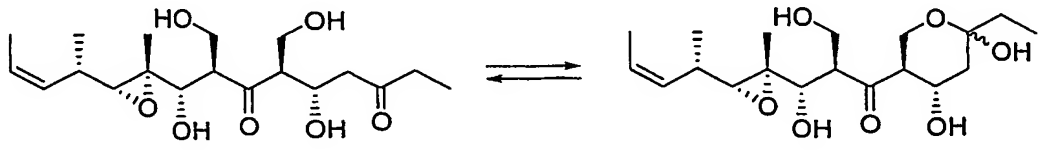
Example 72: Compounds **31b** and **31d**



Following the procedure described in example 50, **30b** (45 mg, 0.054 mmol) was converted to a tautomer equilibrium of **31b** and **31d** (13 mg, 50%, colourless oil) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.59-5.46 (m, 1H), 5.28 (m, 1H), 4.62 (bs, 1H), 4.22 (dd, *J*= 11.5, 11.5 Hz, 1H), 4.10 (dd, *J*= 12.0, 5.0 Hz), 3.70-3.60 (m, 2H), 3.48 (d, *J*= 10.0 Hz, 1H), 3.24-3.17 (m, 1H), 2.94 (ddd, *J*= 11.5, 5.0, 2.0 Hz, 1H), 2.61 (d, *J*= 9.5 Hz, 1H), 2.47-2.41 (m, 1H), 2.03 (dd, *J*= 14.5, 3.5 Hz,), 1.66 (dd, *J*= 7.0, 1.5 Hz, 3H), 1.63-1.61 (m, 2H), 1.58 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.32 (s, 3H), 1.14 (d, *J*= 6.0 Hz, 3H), 0.97 (t, *J*= 7.5 Hz, 3H), 0.87 (s, 9H), 0.15 (s, 3H), 0.00 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 216.3, 130.5, 124.9, 97.2, 78.4, 65.9, 65.2, 62.0, 60.7, 55.7, 55.4, 54.7, 37.1, 34.2, 31.4, 26.0, 18.7, 18.2, 13.3, 11.4, 7.4, -4.3, -5.2.
MS (ESI) m/z: 509 $(M+23)^+$, 451 $(M+1-2xH_2O)^+$.
R_f= 0.42 (Hex:EtOAc, 1:2).

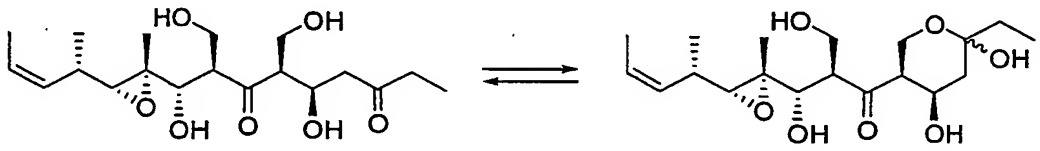
Example 73: Compounds **3c** and **4c**



Following the procedure described in example 52, **31a** (48 mg, 0.058 mmol) was converted to a tautomer equilibrium of **3c** and **4c** (5 mg, 22%) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 0:1).

^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.56-5.49 (m, 1H), 5.28-5.23 (m, 1H), 4.36 (ddd, *J*= 15.0, 11.0, 5.0 Hz, 1H), 3.97-3.66 (m, 4H), 3.62 (d, *J*= 10.0 Hz, 1H), 3.25-3.18 (m, 1H), 2.98 (ddd, *J*= 14.0, 10.0, 4.0 Hz, 1H), 2.78 (d, *J*= 9.0 Hz, 1H), 2.45-2.40 (m, 1H), 2.09 (dd, *J*= 13.0, 5.0 Hz, 1H), 1.67 (q, *J*= 7.5 Hz, 2H), 1.63 (dd, *J*= 1.5 Hz, 7 Hz, 3H), 1.48-1.42 (m, 1H), 1.33 (s, 3H), 1.12 (d *J*= 7.0 Hz, 3H), 0.96 (t, *J*= 7.5 Hz, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) (data of the major product) δ 215.4, 130.0, 125.0, 98.7, 77.3, 67.0, 62.8, 60.8, 60.0, 59.0, 40.1, 35.5, 31.3, 23.9, 19.7, 18.6, 13.3, 11.3, 7.4.
MS (ESI) m/z: 767 $(2xM+23)^+$, 395 $(M+23)^+$, 337 $(M+1-2xH_2O)^+$.
R_f = 0.16 (Hex:EtOAc, 1:2).

Example 74: Compounds **3d** and **4d**



Following the procedure described in example 52, **31b** (150 mg, 0.18 mmol) was converted to a tautomer equilibrium of **3d** and **4d** (10 mg, 15%) after purification of the crude product by flash column chromatography (Hex:EtOAc from 4:1 to 0:1).

^{1}H NMR (500 MHz, CH_3OD) (data of the major product) δ 5.57-5.51 (m, 1H), 5.32-5.26 (m, 1H), 4.80 (m, 1H), 4.26 (dd, *J*= 11.5, 11.5 Hz, 1H), 3.98-3.60 (m, 3H), 3.31-3.29 (m, 1H), 3.24 (d, *J*= 10 Hz,1H), 2.80 (ddd, *J*= 11.5, 4.5, 2.5 Hz, 1H), 2.59 (d, *J*= 9.5 Hz, 1H), 1.95 (dd, *J*= 14.0, 3.5 Hz, 1H), 1.75 (dd, *J*= 14.5, 3.0 Hz, 1H), 1.65 (dd, *J*= 6.5, 15. Hz, 3H), 1.56 (q, *J*= 7.5 Hz, 2H), 1.34 (s, 3H), 1.10 (d, *J*= 7.0 Hz, 3H), 0.92 (t, *J*= 7.5 Hz, 3H).

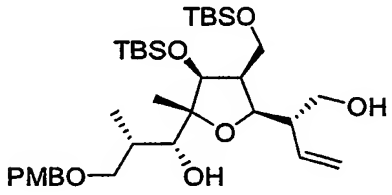
^{1}H NMR (500 MHz, $CDCl_3$) (data of the major product) δ 5.56-5.50 (m, 1H), 5.36 (s, 1H), 5.27-5.21 (m, 1H), 4.76 (bs, 1H), 4.29 (dd, *J*= 11.5, 11.5 Hz, 1H), 3.87 (dd, *J*= 12.5, 4.0 Hz, 1H), 3.73-3.62 (m, 3H), 3.46 (d, *J*= 10.0 Hz,1H), 2.90 (ddd, *J*= 11.5, 4.5, 2.0 Hz, 1H), 2.74 (d, *J*= 9.5 Hz, 1H),2.01 (dd, *J*= 13.5, 3.5 Hz, 1H), 1.70 (dd, *J*=14.0, 2.5 Hz, 1H), 1.62 (dd, *J*= 7.0, 2.0 Hz, 3H), 1.61-1.59 (m, 2H), 1.34 (s, 3H), 1.11 (d, *J*= 6.5 Hz, 3H), 0.95 (t, *J*= 7.0 Hz, 3H).

^{13}C NMR (125 MzH, $CDCl_3$) (data of the major product) δ 214.9, 130.0, 125.1, 96.9, 77.1, 67.1, 65.4, 62.8, 60.9, 55.3, 54.9, 52.7, 37.4, 34.2, 31.3, 18.6, 13.3, 11.4, 7.5.

MS (ESI) m/z: 767.2 $(2xM+23)^+$, 395.3 $(M+23)^+$, 377.3 $(M+23-H_2O)^+$, 337 $(M+1-2xH_2O)^+$, 319.3 $(M+1-3xH_2O)^+$.

R_f = 0.22 (Hex:EtOAc, 1:2).

Example 75: Compound **32**



This compound was obtained as a side product in the preparation of **34** from **11a**. To a solution of **11a** (1.72 g, 2.69 mmol) in acetone (10 mL) was added dimethoxypropane (10 mL) and camphorsulfonic acid (94 mg, 0.4 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (0.56 mL, 4 mmol) was then added and the mixture was stirred for 30 min. Solvents were removed under reduced pressure and the mixture was subjected to flash column chromatography on silica gel (Hex:EtOAc, from 10:1 to 3:1) affording furano **32** (0.6 g, 35%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.8 Hz, 2H), 6.87 (d, *J*= 8.8 Hz, 2H), 5.72-5.65 (m, 1H), 5.09-5.06 (m, 2H), 4.42 (s, 2H), 4.44-4.39 (m, 1H), 3.90 (dd, *J*= 10.0, 2.0 Hz, 1H), 3.84-3.78 (m, 2H), 3.80 (s, 3H), 3.60 (dd, *J*= 6.0, 5.5 Hz, 1H), 3.51-3.42 (m, 3H), 3.36-3.32 (m, 2H), 2.76-2.73 (m, 1H), 2.63-2.58 (m, 1H), 2.13-2.09 (m, 1H), 1.98

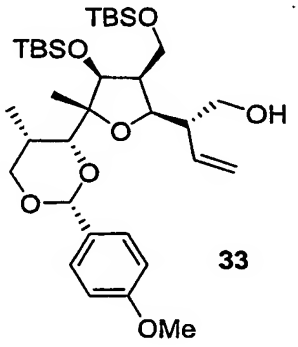
(d, *J*= 4.5 Hz, 1H), 1.02 (d, *J*= 6.8 Hz, 3H), 0.99 (s, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 137.4, 130.5, 129.1, 116.3, 113.7, 83.6, 78.7, 77.7, 77.1, 75.4, 72.7, 64.9, 58.6, 55.2, 49.6, 34.4, 25.8, 25.7, 18.1, 18.0, 17.5, 12.5, -4.7, -5.1, -5.5- .5.6.

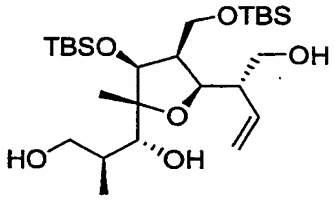
MS (ESI) m/z: 661.4 $(M+23)^+$.

R_f = 0.35 (Hex:EtOAc, 4:1).

Example 76: Compounds **33** and **42**



33



42

To a solution of furane **32** (246 mg, 0.346 mmol) in CH_2Cl_2 (10 mL) and water (0.5 mL) was added 2,3-dichloro-5,6-dicyano1,4-benzoquinone (236 mg, 1.04 mmol) and the reaction mixture was vigorously stirred for 1h at 23 °C. The reaction was hydrolysed by addition of aqueous $NaHCO_3$ (20 mL) and the solution was extracted with CH_2Cl_2 (2x 20mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in MeOH (5 mL) and treated with $NaBH_4$ (30 mg) for 30 min at 23 °C. After this time, solvents were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2, hydrolysed with aqueous NH_4Cl and extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash colum chromatography on silica gel (Hex:EtOAc, from 4:1 to 2:1) to obtain compounds **33** (88 mg, 40%) and **42** (77 mg, 42%) as colourless oils.

33: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82-5.75 (m, 1H), 5.46 (s, 1H), 5.13-5.09 (s, 2H), 4.48 (d, *J*= 6.5 Hz, 1H), 4.07-4.04 (m, 1H), 3.99 (dd, *J*= 4.5, 4.0 Hz, 1H), 3.97-3.94 (m,

1H), 3.91 (d, *J*= 2.5 Hz, 1H), 3.88-3.79 (m, 2H), 3.81 (s, 3H), 3.62 (dd, *J*= 6.0, 5.0 Hz, 1H), 3.50-3.43 (m, 1H), 3.28-3.22 (m, 1H), 2.76-2.67 (m, 2H), 1.76-1.71 (m, 1H), 1.26 (d, *J*= 7.0 Hz, 3H), 1.08 (s, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), -0.07 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 137.4, 131.3, 127.4, 116.3, 113.5, 102.1, 86.4, 83.4, 79.4, 77.0, 75.4, 65.1, 58.7, 55.2, 49.9, 46.2, 30.6, 29.7, 25.8, 18.6, 18.1, 13.3, -4.3, -5.2, -5.4, -5.5.

MS (ESI) m/z: 659.2 $(M+23)^+$.

R_f = 0.31 (Hex:EtOAc, 4:1).

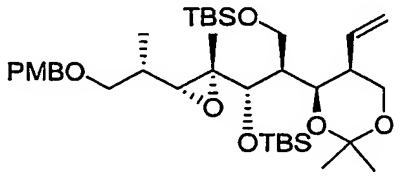
42: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.55 (m, 1H), 5.18-5.12 (m, 2H), 4.41 (d, *J*= 6.7 Hz, 1H), 3.94-3.77 (m, 3H), 3.70-3.36 (m, 3H), 3.14 (d, *J*= 8.6 Hz, 1H), 2.82-2.77 (m, 1H), 2.64-2.59 (m, 1H), 2.04-2.03 (m, 1H), 1.89-1.82 (m, 1H), 1.04 (s, 3H), 0.97 (d, *J*= 6.7 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 6H), 0.09 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 118.4, 82.9, 80.3, 79.7, 79.1, 66.4, 64.7, 58.4, 49.5, 47.0, 39.1, 26.1, 26.0, 18.4, 18.3, 16.5, 15.2, -4.4, -5.0, -5.2, -5.3.

MS (ESI) m/z: 541.2 $(M+23)^+$, 519.3 $(M+1)^+$.

R_f = 0.06 (Hex:EtOAc, 4:1).

Example 77: Compound **34**



To a solution of **11a** (1.72 g, 2.69 mmol) in acetone (10 mL) was added dimethoxypropane (10 mL) and camphorsulfonic acid (94 mg, 0.4 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (0.56 mL, 4 mmol) was then added and the mixture was stirred for 30 min. Solvents were removed under reduced pressure and the mixture was subjected to flash column chromatography on silica gel (Hex:EtOAc, from 10:1 to 3:1) affording acetonide **34** (1.16 g mg, 64%) as a colourless oil.

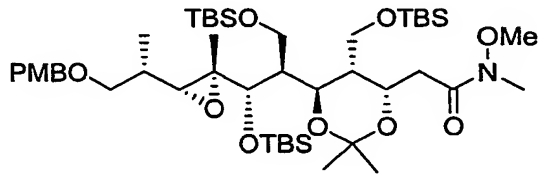
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.4 Hz, 2H), 6.87 (d, *J*= 8.4 Hz, 2H), 6.30-6.17 (m, 1H), 5.13 (dd, *J*= 10.2, 2.1 Hz, 1H), 5.09 (dd, *J*= 16.8, 2.1 Hz, 1H), 4.37 (ss, *J*= 15.6, 1.7 Hz, 2H), 4.19 (dd, *J*= 7.2, 2.1 Hz, 1H), 4.10 (dd, *J*= 11.4, 2.7 Hz, 1H), 3.80 (s, 3H), 3.68 (d, *J*= 6.0 Hz,1H), 3.64-3.57 (m, 2H), 3.49 (dd, *J*= 10.2, 6.0 Hz, 1H), 3.39-3.28 (m, 2H), 2.55 (d, *J*= 9.3 Hz, 1H), 2.27 (d, *J*= 9.6 Hz, 1H), 2.04-1.72 (m, 2H), 1.43 (s, 3H), 1.36 (s, 3H), 1.27 (3, 3H), 1.06 (d, *J*= 6.9 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.12 (s, 3H), 0.07 s, 3H), 0.00 (s, 3H), -0,01 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 137.2, 130.1, 129.1, 117.1, 113.7, 98.8, 76.5, 72.9, 72.7, 67.8, 66.2, 64.8, 64.5, 58.4, 55.2, 44.9, 44.0, 33.5, 29.8, 26.1, 25.9, 18.8, 18.3, 18.0, 14.9, 13.2, -4.5, -4.6, -5.3, -5.5.

MS (ESI) m/z: 701 $(M+23)^+$.

R_f= 0.67 (Hex:EtOAc, 4:1).

Example 78: Compound **35a**

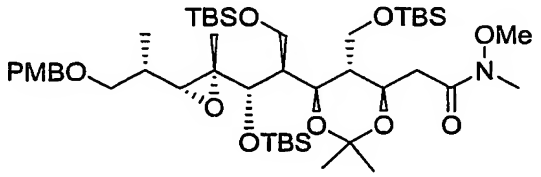


To a solution of **14a** (32 mg, 0.037 mmol) in acetone (1.5 mL) was added dimethoxypropane (1.5 mL) and camphorsulfonic acid (0.85 mg, 0.0037 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (14 μL, 0.01 mmol) was then added and the reaction was stirred for 30 min. Solvents were removed under reduced pressure and the mixture was subjected to flash column chromatography on silica gel (Hex:EtOAc, 4:1) affording acetonide **35a** (27 mg, 81%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J*= 8.8 Hz, 2H), 6,87 (d, *J*= 8.8 Hz, 2H), 4.49-4.38 (m, 3H), 3.82-3.74 (m, 2H), 3.80 (s, 3H), 3.70-3.30 (m 3H), 3.18 (s, 3H), 2.96 (d, *J*= 9.1 Hz, 1H), 2.74-2.60 (m, 1H), 2.52 (d, *J*= 8.6 Hz, 1H), 2.56-2.46 (m, 1H), 2.42-2.36 (m, 1H), 2.04-1.90 (m, 1H), 1.82-1.58 (m 2H), 1.32 (s, 3H), 1.30 (s, 3H), 1.25 (s, 3H), 1.12 (d, *J*= 6.5 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.87 (s, 9H), 0.17 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 159.4, 130.7, 129.4, 114.0, 100.9, 78.2, 73.0, 72.2, 67.2, 65.6, 64.0, 63.4, 61.4, 60.8, 59.8, 55.5, 50.5, 46.5, 39.0, 33.4, 30.0, 26.5, 26.3, 25.2, 25.5, 18.7, 18.4, 18.3, 15.4, 12.0, -3.4, -4.8, -5.2, -5.4, -5.7.
MS (ESI) m/z: 921 $(M+23)^+$.
R_f = 0.24 (Hex:EtOAc, 4:1).

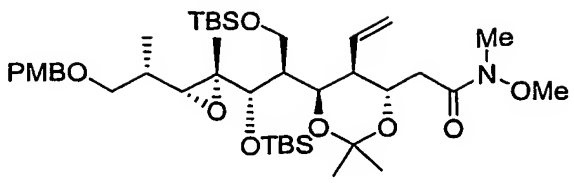
Example 79: Compound **35b**



To a solution of **14b** (40 mg, 0.047 mmol) in acetone (1.5 mL) was added dimethoxypropane (1.5 mL) and camphorsulfonic acid (1 mg, 0.0047 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (14 μL, 0.01 mmol) was then added and the mixture was stirred for 30 min. Solvents were removed under reduced pressure and the mixture was subjected to flash column chromatography on silica gel (Hex:EtOAc, 4:1) affording acetonide **35b** (40 mg, 95%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J*= 8.8 Hz, 2H), 6.87 (d, *J*= 8.8 Hz, 2H), 4.42 (dd, *J*= 22.7, 11.3 Hz, 2H), 4.36-4.20 (m, 1H), 4.05 (d, *J*= 11.5 Hz, 1H), 3.80 (s, 3H), 3.82-3.74 (m, 1H), 3.70 (s, 3H), 3.52-3.42 (m, 4H), 3.38-3.33 (m, 1H) 3.19 (s, 3H), 3.07 (d, *J*= 8.0 Hz, 1H) 2.70 (br s, 1H), 2.48 (d, *J*= 8.6 Hz, 1H), 2.04-1.92 (m, 2H), 1.86-1.76 (m, 1H),1.28 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H), 1.10 (d, *J*= 6.7 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.15 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H).
^{13}CNMR (75 MHz, $CDCl_3$) δ 172.8, 159.4, 130.7, 129.4, 114.0, 97.7, 77.5, 73.1, 72.6, 69.4, 67.7, 64.2, 63.9, 61.7, 61.4, 60.0, 55.5, 47.4, 42.7, 33.3, 30.0, 29.9, 26.4, 26.3, 26.2, 20.2, 18.6, 18.4, 18.3, 15.3, 12.0, -3.4, -3.6, -4.8, -5.2, -5.4, -5.7.
MS (ESI) m/z: 921 $(M+23)^+$.
R_f = 0.27 (Hex:EtOAc, 4:1).

Example 80: Compound **36a**



To a solution of **38a** (26 mg, 0.035 mmol) in acetone (1 mL) was added dimethoxypropane (1 mL) and camphorsulfonic acid (1 mg, 0.0047 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (14 μL, 0.01 mmol) was then added and the mixture was stirred for 30 min. Solvents were removed under reduced pressure and the mixture was subjected to flash chromatography on silica gel (Hex:EtOAc, 3:1) affording acetonide **36a** (18 mg, 70%) as a colourless oil.

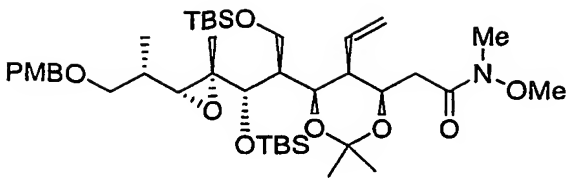
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 5.784-5.71 (m ,1H), 5.11-4.97 (m, 2H), 4.41-4.30 (m, 2H), 4.12 (dd, *J*= 7.0, 5.2 Hz, 1H), 3.96-3.90 (m, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.70-3-61 (m, 2H), 3.46-3.41 (m, 1H), 3.33 (d, *J*= 6.7 Hz, 2H), 3.17 (s, 3H), 2.82-2.74 (m, 1H), 2.56 (d, *J*= 9.3 Hz, 1H), 2.54-2.49 (m, 1H), 2.41-2.34 (m, 1H), 1.85-1.60 (m, 2H), 1.34 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H), 1.07 (d, *J*= 6.7 Hz, 3H), 0.94 (s, 9H), 0.86 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 159.4, 137.1, 130.5, 129.3, 118.7, 114.0, 101.6, 73.1, 72.8, 68.9, 66.2, 65.2, 64.7, 61.4, 59.0, 55.5, 53.5, 43.8, 33.8, 29.9, 26.5, 26.2, 25.0, 24.1, 18.7, 18.3, 15.3, 13.8, -4.1, -4.3, -5.0, -5.1.

MS (ESI) m/z: 802 $(M+23)^+$, 780 $(M+1)^+$.

R_f = 0.18 (Hex:EtOAc, 4:1).

Example 81: Compound **36b**



To a solution of **38b** (34 mg, 0.046 mmol) in acetone (1 mL) were added dimethoxypropane (1 mL) and camphorsulfonic acid (1 mg, 0.0047 mmol) and the mixture was stirred for 1h at 23 °C (until TLC revealed total consumption of the starting material). Et_3N (14 μL, 0.01 mmol) was then added and the reaction was stirred for 30 min at 23 °C. Solvents were removed under reduced pressure and the mixture was subjected to flash column chromatography on silica gel (Hex:EtOAc, 3:1) affording acetonide **36b** (33 mg, 92%) as a colourless oil.

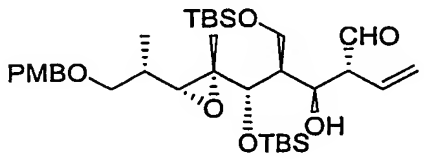
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.95-6.08 (m, 1H), 5.02-5.25 (m, 2H), , 4.42-4.53 (m, 1H), 4.38 (s, 2H), 4.26-4.28 (m, 1H), 3.80 (s, 3H), 3.58-3.69 (m, 2H), 3.65 (s, 3H), 3.41-3.46 (m, 1H), 3.32 (d, J = 6.7 Hz, 2H), 3.14 (s, 3H), 2.59-2.67 (m, 1H), 2.55 (d, J = 9.1 Hz, 1H), 2.31 (d, J = 10.4 Hz, 1H), 2.17-2.29 (m, 1H), 1.64-1.80 (m, 2H), 1.47 (s, 3H), 1.33 (s, 3H), 1,25 (s, 3H), 1.06 (d, J = 6.7 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H), 0.00 (s, 3H), -0.02 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 159.4, 134.5, 130.6, 129.3, 113.9, 99.5, 76.5, 73.0, 72.9, 69.2, 64.4, 61.4, 58.7, 55.4, 48.3, 45.5, 36.6, 33.7, 30.1, 29.9, 26.3, 26.1, 19.7, 18.6, 15.2, 13.6, -4.3, -5.1, -5.2.

MS (ESI) m/z: 780.7 $(M+1)^+$, 802.7 $(M+23)^+$.

R_f = 0.20 (Hex:EtOAc, 4:1).

Example 82: Compound **37**

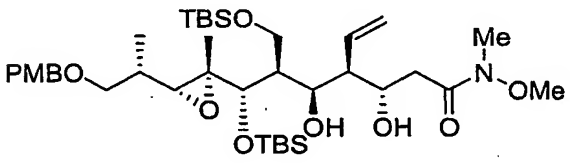


To a solution of diol **11a** (300 mg, 0.47 mmol) in CH_2Cl_2 (10 mL) was added Dess-Martin periodinane (DMP) (0.24 g, 0.56 mmol) and the mixture was stirred at 0 °C for

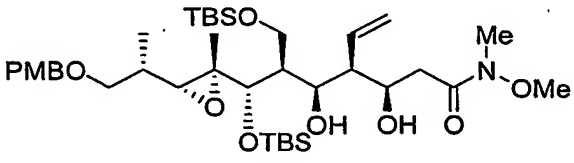
1h and for additional 30 min at 23 °C. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added and the mixture was extracted with CH_2Cl_2 (2x20mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue **37** was used in the next step without further purification.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.45 (d, *J*= 2.6 Hz, 1H), 7.21 (d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 5.75-5.84 (m, 1H), 5.19-5.37 (m, 2H), 4.55-4.58 (m, 1H), 4.40 (s, 2H), 3.81 (s, 3H), 3.45-3.88 (m, 4H), 3.38 (d, *J*= 8.7 Hz, 2H), 3.15-3.20 (m, 1H), 2.55 (d, *J*= 9.1 Hz, 1H), 1.67-1.84 (m, 2H), 1.25 (s, 3H), 1.06 (d, *J*= 6.5 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.16 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).
MS (ESI) m/z: 659.7 (M+23).
R_f = 0.56 (Hex:EtOAc, 4:1).

Example 83: Compounds **38a** and **38b**



38a



38b

To a solution of N-methoxy-N-methyl acetamide (0.158 mL, 1.41 mmol) in dry THF (5 mL) at –78 °C was added lithium bis(trimethylsilyl)amide (1.41 mL, 1.0 M in THF, 1.41 mmol) and the reaction mixture was stirred for 1h at this temperature. Then, a solution of crude aldehyde **37** (0.47 mmol) in THF (10 mL) was added over the previous solution and the reaction mixture was stirred for an additional 1h at –78 °C. Then, a saturated aqueous solution on NH_4Cl (30 mL) was added and the mixture was extracted with EtOAc (3x50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc from 5:1 to 1:1) to yield **38a** and **38b** (38:62) as colourless oils (146 mg, 42 % overall yield for two steps from **11a**).

38a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25(d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 5.81-5.86 (m, 1H), 5.07-5.22 (m, 2H), 4.46-4.50 (m, 1H), 4.44 (dd, *J*= 24.4 and 11.5 Hz, 2H), 4.05-4.16 (m, 1H), 3.65-3.94 (m, 3H), 3.79 (s, 3H), 3.53 (d, *J*= 4.7 Hz, 1H), 3.32-3.44 (m, 2H), 3.15-3.23 (m, 1H), 3.17 (s, 3H), 2.68-2.75 (m, 1H), 2.62 (d, *J*= 9,3 Hz, 1H), 2.18-2.24 (m, 1H), 2.09-2.15 (m, 1H), 1.82-1.93 (m, 2H), 1.24 (s, 3H), 1.04 (d, *J*= 6.7 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 159.3, 139.5, 136.4, 130.7, 129.3, 118.9, 114.0, 77.0, 73.0, 72.7, 69.9, 68.4, 64.9, 64.2, 61.4, 61.3, 55.4, 55.0, 48.7, 36.5, 33.8, 32.1, 29.9, 26.3, 26.0, 18.4, 18.1, 15.1, 14.1, -4.2, -5.0, -5.1, -5.2.

MS (ESI) m/z: 740.5 $(M+1)^+$, 762.6 $(M+23)^+$.

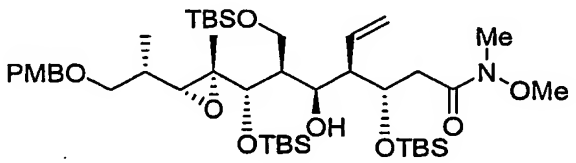
R_f = 0.08 (Hex:EtOAc, 4:1).

38b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23 (d, *J*= 8.6 Hz, 2H), 6.85 (d, *J*= 8.6 Hz, 2H), 5.95-6.08 (m,1H), 5.04-5.30 (m, 2H), 4.43 (dd, *J*= 11.8, 11.8 Hz, 2H), 4.29-4.33 (m, 1H), 4.12 (br s, 1H), 3.78-3.89 (m, 2H), 3.79 (s, 3H), 3.57-3.72 (m, 1H), 3.65 (s, 3H), 3.33-3.44 (m, 2H), 3.15 (s, 3H), 2.59 (d, *J*= 9.1 Hz, 1H), 2.46-2.62 (m, 1H), 1.73-1.89 (m, 2H), 1.24 (s, 3H), 1.06 (d, *J*= 6.7 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.15 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 159.3, 135.4, 130.6, 129.4, 119.2, 113.9, 77.6, 73.0, 72.8, 72.7, 70.3, 64.8, 64.3, 61.4, 60.8, 55.4, 52.8, 47.4, 36.7, 33.6, 29.9, 26.3, 18.4, 18.2, 15.0, 14.0, -4.2, -5.0, -5.1, -5.2.

MS (ESI) m/z: 740.6 $(M+1)^+$, 762.6 $(M+23)^+$.R_f = 0.10 (Hex:EtOAc, 4:1).

Example 84: Compound **39a**



To a solution of **38a** (106 mg, 0.143 mmol) in CH_2Cl_2 (8 mL) at 0°C was added 2,6-lutidine (0.051 mL, 0.44 mmol) and TBSOTf (0.05 mL, 0.22 mmol) successively. The reaction mixture was stirred at this temperature for 1h. Aqueous solution of $NaHCO_3$ (20 mL) was then added and extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **39a** (79 mg, 65%) as a colourless oil.

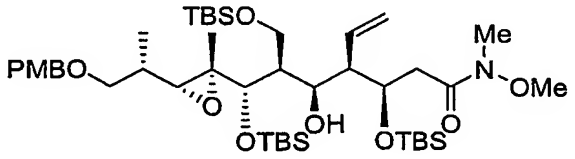
^1H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.6 Hz, 2H), 6.88 (d, *J*= 8.6 Hz, 2H), 5.82-5.94 (m ,1H), 5.07-5.20 (m, 2H), 4.44 (dd, *J*= 18.8, 11.9 Hz, 1H), 4.37-4.41 (m, 2H), 3.91-3.95 (m, 1H), 3.80 (s, 3H), 3.67-3.79 (m, 2H), 3.64 (s, 3H), 3.30-3.40 (m, 2H), 3.13 (s, 3H), 3.07 (d, *J*= 4.4 Hz, 1H), 2.66-2.76 (m, 1H), 2.59 (d, *J* = 9.1 Hz, 1H), 2.47 (dd, *J*= 15.6, 3.4 Hz, 1H), 2.27-2.34 (m, 1H), 1.68-1.82 (m, 2H), 1.25 (s, 3H), 1.05 (d, *J*= 6.7 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.14 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 159.1, 135.8, 130.4, 129.0, 118,4, 113.8, 76.7, 72.9, 72.6, 70.3, 69.0, 64.6, 61.4, 60.4, 56.0, 55.4, 47.3, 33.8, 29.9, 26.4, 26.1, 26.0, 18.5, 18.3, 18.1, 15.2, 14.0, -4.1, -4.2, -4.5, -5.0, -5.1.

MS (ESI) m/z: 854.4 $(M+1)^+$, 876.2 $(M+23)^+$.

R_f = 0.53 (Hex:EtOAc, 4:1).

Example 85: Compound **39b**



To a solution of **38b** (89 mg, 0.12 mmol) in CH_2Cl_2 (8 mL) at 0 °C was added 2,6-lutidine (0.042 mL, 0.36 mmol) and TBSOTf (0.041 mL, 0.18 mmol) successively. The reaction mixture was stirred at this temperature for 1h. A saturated aqueous solution of $NaHCO_3$ (20 mL) was then added and the mixture was extracted with

CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **39b** (86 mg, 84%) as a colourless oil.

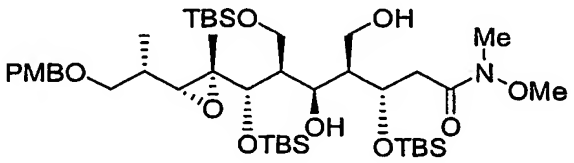
^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 5.89-6.01 (m, 1H), 5.03-5.25 (m, 2H), 4.40 (dd, *J*= 18.4, 11.4 Hz, 2H), 4.16-4.22 (m, 3H), 3.79-3.86 (m, 1H), 3.79 (s, 3H), 3.63-3.70 (m, 1H), 3.67 (s, 3H), 3.27-3.44 (m, 3H), 3.16 (s, 3H), 2.70-2.80 (m, 1H), 2.6 (d, *J*= 9.1 Hz, 1H), 2.51-2.58 (m, 1H), 2.27-2.32 (m 1H), 1.65-1.89 (m, 2H), 1.26 (s, 3H), 1.09 (d, *J*= 6.7 Hz, 3H), 0.92 (s, 9H), 0.87 (s, 9H), 0.86 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 159.4, 137.5, 130.5, 129.5, 118.5, 114.0, 76.4, 73.1, 72.7, 69.1, 64.8, 64.1, 61.5, 61.0, 55.4, 54.4, 44.4, 37.3, 34.4, 32.1, 29.9, 26.6, 26.2, 26.0, 18.9, 18.2, 17.9, 15.4, 12.7, -4.0, -4.2, -4.7, -5.0, -5.1.

MS (ESI) m/z: 854.4 $(M+1)^+$, 876.3 $(M+23)^+$.

R_f = 0.43 (Hex:EtOAc, 4:1).

Example 86: Compound **40a**

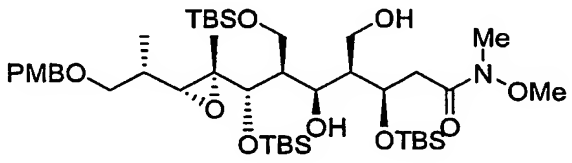


Over a solution of **39a** (79 mg, 0.09 mmol) in CH_2Cl_2 (15 mL) at –78 °C was bubbled ozone until the clear solution turned to light blue (2 min). Then MeOH (15 mL) and $NaBH_4$ (15 mg, 0.4 mmol) were added and the solution was allowed to reach 23 °C during 2h. After this time, solvents were removed under reduced pressure, an the residue was dissolved in CH_2Cl_2, hydrolysed with aqueous NH_4Cl and extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on

silica gel (Hex:EtOAc, from 4:1 to 2:1) to obtain compound **40a** (10 mg, 13%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.6 Hz, 2H), 6.89 (d, *J*= 8.6 Hz, 2H), 4.43 (dd, *J*= 19.6, 11.7 Hz, 2H), 4.20-4.33 (m, 2H), 3.61-4-07 (m, 5H), 3.81 (s, 3H), 3.68 (s, 3H), 3.31-3.45 (m, 2H), 3.16 (s, 3H), 2.77-2.89 (m, 1H), 2.65 (d, *J*= 9.3 Hz, 1H), 2.03-2.16 (m, 2H), 1-76-1.81 (m, 2H), 1.62-1.68 (m, 2H), 1.25 (s, 3H), 1.07 (d, *J*= 6.5 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.00 (s, 3H).
MS (ESI) m/z: 880 $(M+23)^+$.
R_f = 0.15 (Hex:EtOAc, 4:1).

Example 87: Compound **40b**



Over a solution of **39b** (86 mg, 0.1 mmol) in CH_2Cl_2 (15 mL) at –78 °C was bubbled ozone until the clear solution turned to light blue (2 min). Then MeOH (15 mL) and $NaBH_4$ (15 mg, 0.4 mmol) were added and the solution was allowed to reach room temperature during 2h. After this time, solvents were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2, hydrolysed with aqueous NH_4Cl and extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 4:1 to 2:1) to obtain compound **40b** (50 mg, 58%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 (d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 4.41 (dd, *J*= 19.3, 11.4 Hz, 2H), 4.18-4.40 (m, 3H), 3.64-3.95 (m, 6H), 3.79 (s, 3H), 3.71 (s, 3H), 3.30-3.42 (m, 2H), 3.16 (s, 3H), 2.90-2.98 (m, 1H), 2.60 (d, *J* = 9.1 Hz, 1H), 2.55-2.62 (m, 1H), 1.78-1.87 (m, 3H), 1.27 (s, 3H), 1.08 (d, *J*= 6.7 Hz, 3H), 0.92 (s, 9H),

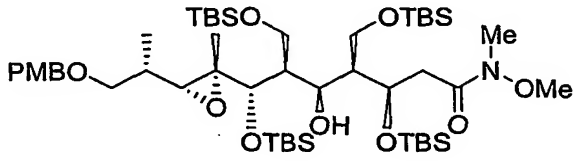
0.86 (s, 9H), 0.85 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 159.2, 130.2, 129.4, 113.8, 75.8, 72.8, 72.5, 72.2, 68.7, 64.5, 63.6, 63.2, 61.4, 60.7, 55.2, 48.5, 43.0, 37.4, 34.2, 31.9, 29.7, 26.3, 25.9, 25.7, 18.6, 17.9, 17.6, 15.2, 12.5, -4.4, -4.5, -5.1, .5.2, -5.4, -5.5.

MS (ESI) m/z: 880 $(M+23)^+$.

R_f = 0.13 (Hex:EtOAc, 4:1).

Example 88: Compound **41b**



To a solution of **40b** (50 mg, 0.06 mmol) in CH_2Cl_2 (8 mL) at 0 °C was added 2,6-lutidine (0.021 mL, 0.18 mmol) and TBSOTf (0.021 mL, 0.09 mmol) successively. The reaction mixture was stirred at this temperature for 1h. A saturated aqueous solution of $NaHCO_3$ (20 mL) was then added and the mixture was extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 10:1) to obtain compound **41b** (57 mg, 98%) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, *J*= 8.6 Hz, 2H), 6.87 (d, *J*= 8.6 Hz, 2H), 4.65 (m, 1H), 4.41 (dd, *J*= 15.9, 11.7 Hz, 2H), 4.17-4.21 (m, 1H), 4.04-4.11 (m, 2H), 3.79-3.86 (m, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.25-3.31 (m, 1H), 3.16 (s, 3H), 2.72-2.84 (m, 1H), 2.62 (d, *J*= 9.3 Hz, 1H), 2.46-2.54 (m, 1H), 1.82-2.05 (m, 1H), 1.62-1.82 (m, 2H), 1.25 (s, 3H), 1.10 (d, *J*= 6.7 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.87 (s, 9H), 0.83 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 159.4, 130.0, 129.4, 114.0, 76.2, 72.8, 72.0, 69.2, 68.7, 64.5, 63.7, 61.9, 61.5, 55.4, 51.2, 44.5, 34.4, 29.9, 26.5, 26.2, 26.1, 18.8, 18.4, 18.1, 17.9, 15.6, 12.3, -3.8, -4.6, -4.7, -5.0, -5.1, -5.2.

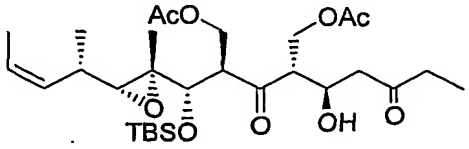
MS (ESI) m/z: 972.6 $(M+1)^+$, 994.6 $(M+23)^+$.

R_f = 0.56 (Hex:EtOAc, 4:1).

Example 89: Compounds **43** and **44**

To a solution of **20b** (14 mg, 0.024 mmol) in $CHCl_3$ (3 mL) was added Et_3N (28 μL, 0.2 mmol) and Ac_2O (10 μL, 0.1 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 16 h. Then, the solvent was eliminated under reduced pressure and the residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 2:1 to 1:1) to obtain pure compounds **43** (6 mg, 47%) as a yellow oil and **44** (6 mg, 44%) as a white solid.

43: ^{1}H NMR (300 MHz, $CDCl_3$) (data of the mayor product) δ 5.53-5.45 (m, 1H), 5.31-5.19 (m, 1H), 4.45-4.40 (m, 2H), 3.92-3.80 (m, 3H), 3.53 (d, *J*= 9.9 Hz, 1H), 3.27-3.21 (m, 1H), 2.76-2.66 (m, 1H), 2.56 (d, *J*= 9.3 Hz, 1H),2.49-2.41 (m, 1H), 2.06-2.00 (m, 1H), 2.03 (s, 3H), 1.68-1.66 (m, 3H), 1.62 (dd, *J*= 12.0, 6.6 Hz, 3H), 1.32 (s, 3H), 1.13 (d, *J*= 6.6 Hz, 3H), 0.97 (t, *J*= 7.5 Hz, 3H), 0.86 (s, 9H), 0.13 (s, 3H), -0.01 (s, 3H).
MS (ESI) m/z: 551 $(M+23)^+$.
Rf = 0.39 (Hex:EtOAc, 50:50).

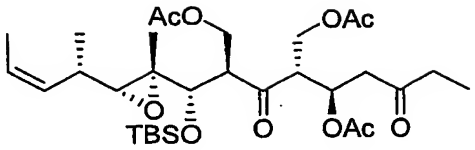


44: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52-5.46 (m, 1H), 5.22-5.15 (m, 1H), 4.50 (dd, *J*= 11.0, 4.5 Hz, 1H), 4.47-4.43 (m, 1H), 4.34-4.33 (m, 1H) 4.13-4.07 (m, 1H), 3.90-3.81 (m, 1H), 3.70-3.65 (m, 1H), 3.56 (d, *J*= 9.3 Hz, 1H), 3.33-3.26 (m, 1H), 3.13-3.11 (m, 1H), 2.69-2.64 (m, 2H), 2.55 (d, *J*= 9.0 Hz, 1H),2.48-2.39 (m, 2H), 2.09 (s, 3H), 2.00 (s, 3H), 1.67-1.61 (m, 3H), 1.32 (s, 3H), 1.13 (d, *J*= 6.3 Hz, 3H), 1.05 (t, *J*= 7.2 Hz, 3H), 0.85 (s, 9H), 0.15 (s, 3H), -0.01 (s, 3H).

MS (ESI) m/z: 593 $(M+23)^+$.

Rf = 0.53 (Hex:EtOAc, 50:50).

Example 90: Compound **45**



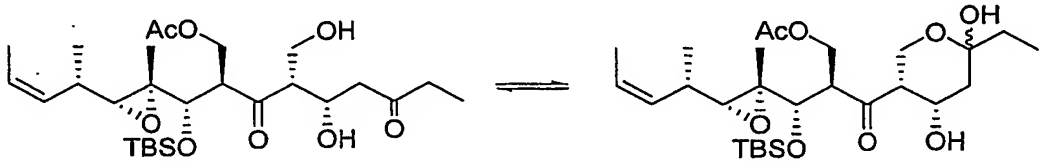
To a solution of **20b** (34 mg, 0.07 mmol) in CH_2Cl_2 (0.7 mL) was added Et_3N (11.5 μL, 0.82 mmol), DMAP (5 mg, 0.041 mmol) and Ac_2O (39 μL, 0.41 mmol) at 0 °C. The reaction mixture was stirred at 23 °C for 3 h. Then, 0.1N HCl was added until pH= 4-5, and the reaction was extracted with CH_2Cl_2 (2x5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, 3:1) to obtain compound **45** (17 mg, 40%) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60-5.56 (m, 1H), 5.54-5.44 (m, 1H), 5.26-5.19 (m, 1H), 4.46 (dd, *J*= 11.1, 5.7 Hz, 1H), 4.35 (dd, *J*= 11.4, 3.3 Hz, 1H), 4.14 (dd, *J*= 12.0, 6.9 Hz, 1H), 3.87 (dd, *J*= 11.4, 8.1 Hz, 1H), 3.55-3.49 (m, 2H), 3.46-3.38 (m, 2H),2.79-2.76 (m, 2H), 2.52 (d, *J*= 9.3 Hz, 1H),2.45-2.38 (m, 3H), 2.06 (s, 3H), 1.99 (s, 6H), 1:62 (dd, *J*= 6.9, 1.8 Hz, 1H), 1.33 (s, 3H), 1.11 (d, *J*= 6.3 Hz, 3H), 1.03 (t, *J*= 7.2 Hz, 3H), 0.85 (s, 9H), 0.13 (s, 3H), 0.00 (s, 3H).

MS (ESI) m/z: 635 $(M+23)^+$.

Rf = 0.54 (Hex:EtOAc, 50:50).

Example 91: Compound **46**

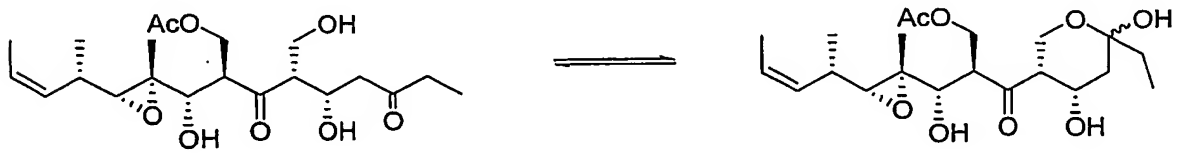


To a solution of **20a** (18 mg, 0.037 mmol) in CH_2Cl_2 (3 mL) was added Et_3N (21 μL, 0.15 mmol) and Ac_2O (7 μL, 0.074 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 16 h. Then, $NaHCO_3$ (5 mL) was added and the reaction was extracted with CH_2Cl_2 (2x5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 3:1 to 2:1) to obtain compound **46** (16 mg, 82%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) (data of the mayor product) δ 5.55-5.45 (m, 1H), 5.26-5.19 (m, 1H), 5.06 (s, 1H), 4.56 (bs, 1H), 4.45 (dd, *J*= 11.4, 3.6 Hz, 1H), 4.22 (t, *J*= 11.7 Hz, 1H), 4.06 (bs, 1H), 3.97-3.82 (m, 2H), 3.47 (d, *J*= 9.6 Hz, 1H), 3.21-3.14 (m, 1H), 2.94-2.89 (m, 1H), 2.56 (d, *J*= 9.0 Hz, 1H),2.06-2.98 (m, 1H), 2.02 (s, 3H), 1.63-1.58 (m, 6H), 1.30 (s, 3H), 1.13 (d, *J*= 6.6 Hz, 3H), 0.94 (t, *J*= 7.5 Hz, 3H), 0.85 (s, 9H), 0.13 (s, 3H), -0.01 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) (data of the mayor product) δ 212.2, 170.4, 130.5, 125.3, 97.5, 77.5, 66.0, 65.6, 62.2, 62.1, 55.9, 54.2, 54.1, 37.4, 34.6, 31.6, 29.9, 26.2, 20.9, 18.9, 13.5, 11.8, 7.7, -4.2, -4.6.
MS (ESI) m/z: 551 $(M+23)^+$.
Rf = 0.38 (Hex:EtOAc, 2:1).

Example 92: Compounds **47** and **1**

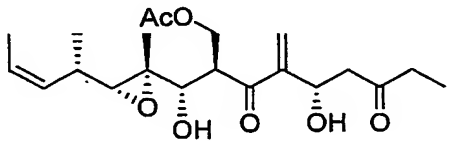
To a solution of crude **4a** (20 mg, 0.054 mmol) in $CHCl_3$ (3 mL) was added Et_3N (22 μL, 0.16 mmol) and Ac_2O (8 μL, 0.081 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 16 h. Then, the solvent was eliminated under reduced pressure and the residue was purified by flash column chromatography on silica gel (Hex:EtOAc, from 2:1 to 1:1) to obtain pure compounds **47** (10 mg, 48%) and **1** (4 mg, 44%) as yellow oils.



47: ^{1}H NMR (500 MHz CD_3OD) (data of the hemiketal product) δ 5.50 (m, 1H), 5.26 (m, 1H), 4.57 (m, 1H), 4.28 (dd, *J*= 12.5, 12.0 Hz, 1H), 4.15 (dd, *J*= 11.0, 4.0 Hz, 1H), 4.00 (dd, *J*= 11.0, 9.5 Hz, 1H), 3.69 (dd, *J*= 12.5, 5.0 Hz, 1H), 3.40 (m, 1H), 3,13 (d, *J*= 10.5 Hz, 1H), 2.97 (ddd, *J*= 12.0, 5.0, 2.5 Hz, 1H), 2.62 (d, *J*= 9.5 Hz, 1H), 2.47 (m, 1H), 1.97 (s, 3H), 1.93 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.72 (dd, *J*= 14.0, 3.0 Hz, 1H), 1.64 (brd, *J*= 7.0 Hz, 3H), 1.57 (d, *J*= 7.5 Hz, 2H), 1.37 (s, 3H), 1.09 (d, *J*= 7.0 Hz, 3H), 0.92 (t, *J*= 7.5 Hz, 3H).

^{13}C NMR (125 MHz CD_3OD) (data of the hemiketal product) δ 212.6, 172.6, 131.5, 126.1, 98.8, 78.6, 67.6, 66.1, 64.3, 62.9, 56.8, 56.0, 52.2, 38.6, 35.6, 32.3, 20.8, 18.8, 13.6, 11.6, 7.9.

MS (ESI) m/z: 437 $(M+23)^+$.



1: ^{1}H NMR (500 MHz MeOD) δ 6.27 (s, 1H), 6.22 (d, *J*= 1.2 Hz, 1H), 5.55-5.46 (m, 1H), 5.30-5.23 (m, 1H), 5.04-5.01 (m, 1H), 4.32 (dd, *J*= 10.5, 3.9 Hz, 1H), 3.88 (dd, *J*= 9.9, 9.9 Hz, 1H), 3.76 (ddd, *J*= 19.8, 9.9, 3.6 Hz 1H), 3.34 (d, *J*= 9.9 Hz), 1.94 (s, 3H), 1.65 (dd, *J*= 6.9, 1.8 Hz, 1H), 1.38 (d, *J*= 6.6 Hz, 3H), 1.01 (t, *J*= 7.5 Hz, 3H).

MS (ESI) m/z: 419 $(M+23)^+$.

Rf = 0.37 (Hex:EtOAc, 1:2).

Example 93: Bioassays For Antitumor Screening

The finality of these assays is to interrupt the growth of a "*in vitro*" tumor cell culture by means a continued exhibition of the cells to the sample to be testing.

Cell Lines

NAME	N° ATCC	SPECIES	TISSUE	CHARACTERISTICS
K-562	CCL-243	human	leukemia	erythroleukemia (pleural effusion)
A-549	CCL-185	human	lung	lung carcinoma "NSCL"
SK-MEL-28	HTB-72	human	melanoma	malignant melanoma
HT-29	HTB-38	human	colon	colon adenocarcinoma
LoVo	CCL-229	human	colon	colon adenocarcinoma
LoVo-Dox		human	colon	colon adenocarcinoma (MDR)
DU-145	HTB-81	human	prostate	prostate carcinoma, not androgen receptors
LNCaP	CRL-1740	human	prostate	prostate adenocarcinoma, with androgen receptors
SK-BR-3	HTB-30	human	breast	breast adenocarcinoma, Her2/neu+, (pleural effusion)
IGROV		human	ovary	ovary adenocarcinoma
IGROV-ET		human	ovary	ovary adenocarcinoma, characterized as ET-743 resistant cells
HeLa	CCL-2	human	cervix	cervix epitheloid carcinoma
HeLa-APL	CCL-3	human	cervix	cervix epitheloid carcinoma, characterized as aplidine resistant cells
PANC-1	CRL-1469	human	pancreas	pancreatic epitheloid carcinoma

Inhibition of cell growth by colorimetric assay.

A colorimetric type of assay, using sulforhodamine B (SRB) reaction has been adapted for a quantitative measurement of cell growth and viability (following the technique described by P. A. Skehan, *et al.*, *J. Natl. Cancer Inst.* **1990**, *82*, 1107-1112).

This form of assay employs 96 well cell culture microplates of 9 mm diameter (T. Mosmann *et al.*, *J. of Immunological Methods* **1983**, *65*, 55-63; G. T. Faircloth *et al.*, *J. of*

Tissue and Culture Methods **1988,** *11*, 201-205). Most of the cell lines are obtained from American Type Culture Collection (ATCC) derived from different human cancer types.

Cells are maintained in RPMI 1640 10% FBS, supplemented with 0.1 g/L penicillin and 0.1 g/L streptomycin sulfate and then incubated at 37°C, 5% CO_2 and 98% humidity. For the experiments, cells were harvested from subconfluent cultures using trypsin and resuspended in fresh medium before plating.

Cells are seeded in 96 well microtiter plates, at 5 x 10^3 cells per well in aliquots of 195 µL medium, and they are allowed to attach to the plate surface by growing in drug free medium for 18 hours. Afterward, samples are added in aliquots of 5 µL in a ranging from 10 to 10^{-8} µg/mL, dissolved in DMSO/EtOH/PBS (0.5:0.5:99). After 48 hours exposure, the antitumor effect are measured by the SRB methodology: cells are fixed by adding 50 µL of cold 50% (wt/vol) trichloroacetic acid (TCA) and incubated for 60 minutes at 4°C. Plates are washed with deionised water and dried. One hundred µl of SRB solution (0.4% wt/vol in 1% acetic acid) is added to each microtiter well and incubated for 10 minutes at room temperature. Unbound SRB is removed by washing with 1% acetic acid. Plates are air dried and bound stain is solubilized with Tris buffer. Optical densities are read on a automated spectrophotometric plate reader at a single wavelength of 490 nm.

The values for mean +/- SD of data from triplicate wells are calculated. Some parameters for cellular responses can be calculated: GI = growth inhibition, TGI = total growth inhibition (cytostatic effect) and LC = cell killing (cytotoxic effect).

Tables 1 illustrates data on the biological activity of the compounds of the present invention.

Table 1: Activity data (Molar)

		19a	19b	20a+20c	20b+20d	31b+31d
DU-145	GI50	1,21E-05	1,20E-05	1,07E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
LN-caP	GI50	1,21E-05	1,20E-05	8,42E-06	1,24E-05	-
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	-
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	-
IGROV	GI50	1,21E-05	1,20E-05	1,41E-05	2,05E-05	1,65E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
IGROV-ET	GI50	1,21E-05	1,20E-05	1,38E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
SK-BR-3	GI50	1,21E-05	6,15E-06	1,11E-05	1,49E-05	2,02E-05
	TGI	1,21E-05	1,17E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
MEL-28	GI50	1,21E-05	1,20E-05	1,63E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
A-549	GI50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
K-562	GI50	1,21E-05	1,20E-05	7,75E-06	1,03E-05	-
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	-
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	-
PANC-1	GI50	1,21E-05	1,20E-05	1,40E-05	9,37E-06	1,26E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
HT-29	GI50	1,21E-05	1,20E-05	1,71E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05

	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
LOVO	GI50	1,21E-05	1,20E-05	1,04E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
LOVO-DOX	GI50	1,21E-05	1,20E-05	8,51E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
HELA	GI50	1,21E-05	1,20E-05	1,33E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
HELA-APL	GI50	1,21E-05	1,20E-05	1,29E-05	2,05E-05	2,05E-05
	TGI	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05
	LC50	1,21E-05	1,20E-05	2,05E-05	2,05E-05	2,05E-05

Table 1 (cont.): Activity data (Molar)

		30a	30b	3a+4a	3b+4b	3c+4c	3d+4d
DU-145	GI50	1,21E-05	1,21E-05	6,31E-08	6,52E-06	5,50E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	4,03E-07	2,68E-05	4,16E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	2,03E-06	2,68E-05	2,68E-05	2,68E-05
LN-caP	GI50	-	-	8,19E-08	9,29E-06	7,03E-07	-
	TGI	-	-	5,53E-07	2,68E-05	4,56E-06	-
	LC50	-	-	5,32E-06	2,68E-05	2,68E-05	-
IGROV	GI50	-	-	7,30E-08	5,96E-06	5,53E-07	2,05E-05
	TGI	-	-	3,76E-07	2,68E-05	3,57E-06	2,68E-05
	LC50	-	-	3,92E-06	2,68E-05	2,09E-05	2,68E-05
IGROV-ET	GI50	8,27E-06	8,27E-06	1,00E-07	6,55E-06	7,03E-07	1,71E-05
	TGI	1,21E-05	1,21E-05	1,07E-06	2,68E-05	6,95E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	2,68E-05	2,68E-05	2,68E-05	2,68E-05
SK-BR-3	GI50	8,56E-06	1,21E-05	3,03E-08	5,07E-06	1,16E-06	2,05E-05
	TGI	1,21E-05	1,21E-05	4,75E-07	1,09E-05	6,07E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	5,34E-06	2,33E-05	2,68E-05	2,68E-05

MEL-28	GI50	1,21E-05	1,21E-05	7,54E-08	5,53E-06	6,34E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	8,32E-07	2,68E-05	7,25E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	1,20E-05	2,68E-05	2,68E-05	2,68E-05
A-549	GI50	1,21E-05	1,21E-05	1,44E-07	2,68E-05	9,13E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	2,59E-06	2,68E-05	1,34E-05	2,68E-05
	LC50	1,21E-05	1,21E-05	1,56E-05	2,68E-05	2,68E-05	2,68E-05
K-562	GI50	-	-	5,21E-07	1,42E-05	4,59E-06	-
	TGI	-	-	1,46E-06	1,82E-05	1,19E-05	-
	LC50	-	-	8,40E-06	2,33E-05	2,68E-05	-
PANC-1	GI50	1,21E-05	1,21E-05	8,97E-08	2,68E-05	1,03E-06	1,35E-05
	TGI	1,21E-05	1,21E-05	2,95E-06	2,68E-05	1,33E-05	2,68E-05
	LC50	1,21E-05	1,21E-05	2,68E-05	2,68E-05	2,68E-05	2,68E-05
HT-29	GI50	-	-	6,01E-08	2,21E-05	5,64E-07	2,68E-05
	TGI	-	-	1,18E-06	2,68E-05	6,69E-06	2,68E-05
	LC50	-	-	2,68E-05	2,68E-05	2,68E-05	2,68E-05
LOVO	GI50	6,37E-06	6,88E-06	8,22E-08	4,81E-06	7,14E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	1,35E-06	1,26E-05	7,01E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	1,77E-05	2,68E-05	2,68E-05	2,68E-05
LOVO-DOX	GI50	1,21E-05	1,21E-05	1,52E-07	9,34E-06	8,46E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	1,36E-06	2,68E-05	6,18E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	2,68E-05	2,68E-05	2,68E-05	2,68E-05
HELA	GI50	1,21E-05	1,21E-05	7,28E-08	8,73E-06	6,20E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	5,50E-07	2,68E-05	4,78E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	7,14E-06	2,68E-05	2,68E-05	2,68E-05
HELA-APL	GI50	1,21E-05	1,21E-05	7,33E-08	5,18E-06	5,93E-07	2,68E-05
	TGI	1,21E-05	1,21E-05	9,83E-07	2,68E-05	8,67E-06	2,68E-05
	LC50	1,21E-05	1,21E-05	1,47E-05	2,68E-05	2,68E-05	2,68E-05

Table 1 (cont.): Activity data (Molar)

		46	43	44	45	47	1
DU-145	GI50	9,65E-06	4,99E-06	4,99E-06	1,63E-05	8,15E-08	3,66E-06
	TGI	1,89E-05	9,66E-06	1,04E-05	1,63E-05	5,31E-07	1,02E-05
	LC50	1,89E-05	1,87E-05	1,75E-05	1,63E-05	2,41E-05	2,52E-05
LN-caP	GI50	5,24E-06	3,78E-06	3,77E-06	8,34E-06	8,13E-08	1,45E-06
	TGI	9,06E-06	7,62E-06	7,88E-06	1,63E-05	5,36E-07	6,31E-06
	LC50	1,56E-05	1,54E-05	1,66E-05	1,63E-05	8,88E-06	2,52E-05
IGROV	GI50	7,74E-06	4,94E-06	4,13E-06	1,63E-05	6,39E-08	1,63E-06
	TGI	1,89E-05	9,99E-06	7,67E-06	1,63E-05	5,28E-07	5,67E-06
	LC50	1,89E-05	1,89E-05	1,42E-05	1,63E-05	2,41E-05	1,76E-05
IGROV-ET	GI50	7,39E-06	4,52E-06	4,15E-06	1,58E-05	1,52E-07	3,10E-06
	TGI	1,89E-05	8,96E-06	8,09E-06	1,63E-05	1,08E-06	8,58E-06
	LC50	1,89E-05	1,78E-05	1,58E-05	1,63E-05	2,41E-05	2,37E-05
SK-BR-3	GI50	-	-	-	-	2,31E-08	4,69E-07
	TGI	-	-	-	-	1,18E-07	1,11E-05
	LC50	-	-	-	-	2,30E-06	3,43E-06
MEL-28	GI50	9,89E-06	3,90E-06	3,84E-06	1,63E-05	8,20E-08	2,72E-06
	TGI	1,89E-05	7,24E-06	6,96E-06	1,63E-05	9,84E-07	6,10E-06
	LC50	1,89E-05	1,34E-05	1,26E-05	1,63E-05	1,29E-05	1,36E-05
A-549	GI50	1,34E-05	4,44E-06	4,01E-06	1,63E-05	1,51E-07	1,10E-06
	TGI	1,89E-05	8,49E-06	7,87E-06	1,63E-05	1,12E-06	5,04E-06
	LC50	1,89E-05	1,62E-05	1,54E-05	1,63E-05	2,32E-05	2,35E-05
K-562	GI50	1,20E-05	3,59E-06	6,10E-06	1,63E-05	2,94E-07	1,99E-06
	TGI	1,89E-05	7,72E-06	1,14E-05	1,63E-05	9,99E-07	7,36E-06
	LC50	1,89E-05	1,65E-05	1,75E-05	1,63E-05	1,18E-05	2,46E-05
PANC-1	GI50	7,38E-06	3,73E-06	3,73E-06	8,24E-06	9,05E-08	3,33E-06
	TGI	1,89E-05	7,02E-06	7,20E-06	1,63E-05	2,38E-06	8,40E-06
	LC50	1,89E-05	1,32E-05	1,38E-05	1,63E-05	1,95E-05	2,13E-05
HT-29	GI50	1,50E-05	4,24E-06	6,22E-06	1,63E-05	1,06E-07	1,67E-06
	TGI	1,89E-05	8,28E-06	1,75E-05	1,63E-05	3,11E-06	5,37E-06
	LC50	1,89E-05	1,62E-05	1,70E-05	1,63E-05	2,41E-05	1,34E-05

LOVO	GI50	4,37E-06	4,03E-06	4,05E-06	8,26E-06	4,03E-08	1,62E-06
	TGI	1,00E-05	9,06E-06	8,99E-06	1,63E-05	3,74E-07	4,87E-06
	LC50	1,89E-05	1,89E-05	1,75E-05	1,63E-05	1,77E-05	1,26E-05
LOVO-DOX	GI50	6,15E-06	3,31E-06	4,27E-06	1,05E-05	2,16E-07	3,13E-06
	TGI	1,89E-05	7,21E-06	8,90E-06	1,63E-05	2,41E-05	8,10E-06
	LC50	1,89E-05	1,57E-05	1,75E-05	1,63E-05	2,41E-05	2,11E-05
HELA	GI50	8,81E-06	4,37E-06	3,91E-06	1,63E-05	7,17E-08	1,99E-06
	TGI	1,89E-05	8,47E-06	7,59E-06	1,63E-05	4,34E-07	6,66E-06
	LC50	1,89E-05	1,64E-05	1,47E-05	1,63E-05	1,35E-05	2,05E-05
HELA-APL	GI50	1,01E-05	4,27E-06	3,77E-06	1,63E-05	7,96E-08	1,72E-06
	TGI	1,89E-05	9,34E-06	9,83E-06	1,63E-05	5,91E-07	6,23E-06
	LC50	1,89E-05	1,89E-05	1,75E-05	1,63E-05	2,41E-05	2,20E-03